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THE

MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—10TH YEAR. SYDNEY: SATURDAY, JUNE 16, 1923. No. 24.

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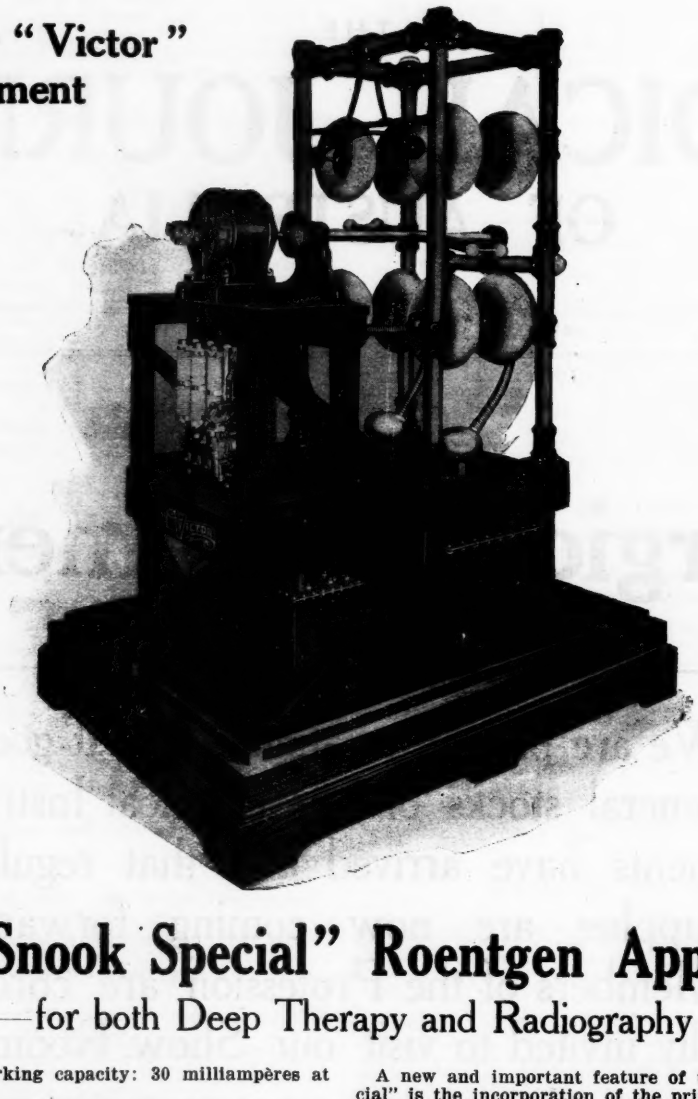

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1923.

THE MEDICAL JOURNAL OF AUSTRALIA

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THE LEUCOCYTES IN HEALTH AND IN DISEASE.[1]

BY K. DOUGLAS FAIRLEY, M.D.,
John Grice Cancer Research Scholar.

(From the Walter and Eliza Hall Institute of Research, Melbourne.)

IT is obviously impossible to diagnose abnormal conditions of the blood until one is familiar with the physiological variations in the normal individual. Much of the accepted teaching with regard to normal blood must be considerably modified in the light of more recent observations.

THE LEUCOCYTES OF NORMAL BLOOD.

The white blood corpuscles of normal blood are usually classified as:

(*i.*) Granular leucocytes, *id est*, polymorpho-nuclear cells: (*a*) neutrophile, (*b*) eosinophile, (*c*) basophile.

(*ii.*) Non-granular leucocytes, *id est*, mononuclear cells: (*a*) lymphocytes, small and large; (*b*) endothelial leucocytes, large mononuclear and transitional cells.

The morphology of most of these cells is too well known to need description.

Only two difficulties arise in the examination of the white corpuscles in the blood film of a normal adult. These difficulties are to differentiate between the large lymphocyte and the large mononuclear cell and again between the transitional cell and the earliest form of polymorpho-nuclear neutrophile cell, the so-called metamyelocyte.

The large lymphocyte is usually smaller than the ordinary polymorpho-nuclear neutrophile cell, varying from 8 μ to 11 μ in diameter. The nucleus is round, usually central, with a fairly deep, rich violet stain, sharply marked off from and relatively large compared with the amount of the cytoplasm, which is a clear glass-like, translucent pale blue, sometimes containing large pinkish azure granules.

The large mononuclear cell is somewhat larger, being 10 μ to 20 μ in diameter. The nucleus is oval, vesicular, eccentric, faintly staining, not sharply marked off from and small compared with the amount of the cytoplasm, which is a somewhat opaque lilac or greyish blue tint, the opacity suggesting frosted glass rather than the clear glass-like appearance of the lymphocyte.

The zone of cytoplasm is usually wide at some

[1] Read at a meeting of the Victorian Branch of the British Medical Association on May 2, 1923.

part as a result of the indentation or eccentric position of the nucleus, while a few granules may be present.

The faint staining of the nucleus, which is rarely both round and centrally placed, and the opaque lilac of the cytoplasm, are the chief features distinguishing this cell from the large lymphocyte.

McJunkin, in a series of interesting studies on these endothelial cells, concludes that, owing to their similarity to large lymphocytes, it is impossible accurately to identify all the large mononuclear cells by any of the blood stains in common use. He and Charlton[1] have introduced an easy and effective staining method by which these cells can be identified.

The transitional cells are usually regarded as older forms of large mononuclear cells, which they resemble in most respects, though the nucleus is kidney-shaped and the protoplasm stains less intensely. These comprise the largest forms found in normal blood.

The so-called neutrophile metamyelocytes (the earliest forms of neutrophile polymorpho-nuclear cells found in normal blood) are smaller cells with more eosinophilic cytoplasm containing numerous fine neutrophile granules and a more pyknotic nucleus.

The Total and Differential White Cell Counts in Normal Adult Blood.

Of late years many investigators in different countries have shown that the old accepted proportion of three to one was not correct as regards the polymorpho-nuclear and the mononuclear leucocytes in normal blood.

The normal range of variations differs probably in different countries and with different races. It must be realized that the blood cell formula is relatively unstable from hour to hour in the same individual and a difference of 10% or 15% in the polymorpho-nuclear neutrophile or lymphocytic cells usually has little significance. The leucocyte count is altered according as the blood is taken from the finger or ear, while the patient is erect or recumbent, in a state of fasting or digestion and with a temporary cessation of or increased amplitude of respiratory movements. Mauriac and Cabouat[2] made numerous observations on their own bloods from 8 a.m. to 8 p.m. and concluded that in the normal individual the number of leucocytes per cubic millimetre varies from one moment to another, the variations being least on getting up in the morning, greatest between 3 p.m. and 9 p.m., when variations from 6,500 to 12,300 per cubic millimetre may occur within half an hour. This explains the widely different estimates of digestive leucocytosis, the term digestive oscillations being preferable.

The percentage of polymorpho-nuclear neutrophile cells varied from 47% to 73% in one of them and from 47% to 67% in the other.

No examination of the leucocytes of the blood is complete unless the absolute numbers per cubic millimetre of the various leucocytes are given, as well as their relative percentages. It is frequently forgotten that an increase in the percentage of lymphocytes present in the blood may mean either an increase or even a decrease in the absolute numbers of circulating lymphocytes or a normal total number of these cells, the true interpretation of the examination in all but the former being a diminution in the number of circulating polymorpho-nuclear neutrophile cells.

Thirty-six total and differential leucocyte counts were done on twenty-nine apparently normal young adult male and female doctors, nurses and students at the Melbourne Hospital. The blood was obtained from the finger, several slides being taken in each case, so that if any uneven distribution of the leucocytes occurred the film was rejected. Daniels's method of spreading was used, the blood being drawn out behind the slide, thus giving an evenly-spread film and avoiding crushing or distortion of the cells. Moderately thick films were used to facilitate counting, at least six hundred cells being counted in every case and where there was any marked deviation from the average, one thousand to fourteen hundred cells were enumerated.

The results of this investigation are shown in Tables I., II. and III..

Table I. gives the normal blood formula according to various recent investigators.

TABLE I.—THE NORMAL BLOOD FORMULA.

Observers.	Date.	Polymorpho-nuclear Cells.	Mononuclear Cells.	Remarks.
Tate and McLeod[3]	1919	49.5%	50.2%	Fasting
V. Bonsdorff	1914	48.0%	52.0%	Fasting
Türk[4]	1912	58.1%	41.9%	——
Zappa[5]	1920	61.0%	39.0%	——
Fairley	1922	56.4%	43.6%	At various times from 8.30 a.m. to 10 p.m.
Average		54.6%	45.3%	

Table I. forcibly illustrates that the accepted teaching of the normal proportions of polymorpho-nuclear to mononuclear cells requires revision.

Table II. shows the average minimum and maximum, relative and absolute leucocyte counts in this series, while Table III. illustrates the leucocyte counts in the individual examinations.

Many interesting facts are manifest in these tables.

Polymorpho-nuclear neutrophile cells fall between 50% and 70% in about three-fourths of these counts; in the remainder they vary between 37% and 50%.

In all but one individual the total counts varied between 2,500 and 7,000 neutrophile cells per cubic millimetre, over half being below 5,000 per cubic millimetre.

In the one exception on two separate occasions nine weeks apart, the count was 8,750 and 18,880 neutrophile cells per cubic millimetre.

The limits of variation of the polymorpho-nuclear neutrophile count in the normal adult are obviously great, varying probably between 30% and 80% and

between 2,000 and 10,000 neutrophiles per cubic millimetre.

The normal upper limits for eosinophile cells are usually stated as 4% and 250 or 300 per cubic millimetre. In only two patients in this series were these absolute numbers exceeded; in one the number was 315, in the other there were 200 and 400 eosinophile cells per cubic millimetre on different occasions.

The basophile cells fell within the accepted nor-

TABLE II.—THE AVERAGE, MINIMUM AND MAXIMUM LEUCOCYTE COUNTS IN TWENTY-NINE NORMAL ADULTS.

Leucocytes.	Twenty Counts on Fifteen Females.						Sixteen Counts on Fourteen Males.						Thirty-Six Counts on Twenty-Nine People.	
	Percentage.			Absolute Numbers Per Cubic Millimetre.			Percentage.			Absolute Numbers Per Cubic Millimetre.			Percentage.	Absolute Numbers Per Cubic Millimetre
	Average.	Minimum.	Maximum.	Average.	Minimum.	Maximum.	Average.	Minimum.	Maximum.	Average.	Minimum.	Maximum.	Average.	Average.
Polymorpho-nuclear Neutrophile Cells ..	57.6	38.2	69.8	5,400	3,700	8,800	51.2	37.0	64.3	4,250	2,525	6,420	54.5	4,825
Polymorpho-nuclear Eosinophile Cells ..	1.6	0.3	3.2	150	20	315	1.5	0.7	3.3	120	35	400	1.5	130
Polymorpho-nuclear Basophile Cells ..	0.4	—	1.1	35	—	100	0.4	0.2	1.0	35	15	80	0.4	35
Lymphocytes, Small and Large	36.1	26.0	54.8	3,380	1,650	6,050	42.4	30.4	58.2	3,520	2,450	6,350	39.1	3,460
Large Mononuclear and Transitional Cells	4.3	1.6	7.0	400	125	725	4.6	2.3	6.3	400	200	750	4.5	400
Total	—	—	—	9,370	6,300	13,500	—	—	—	8,300	5,250	12,200	—	8,850

TABLE III.—PERCENTAGE AND ABSOLUTE NUMBERS OF LEUCOCYTE COUNTS ON INDIVIDUAL CASES.

Females.

Number of Case.	Time of Day.	Total Count.	Percentage.					Total Number of Cells Per Cubic Millimetre.				
			Polymorphonuclear Neutrophile Cells.	Polymorphonuclear Eosinophile Cells.	Polymorphonuclear Basophile Cells.	Lymphocytes, Small and Large.	Large Mononuclear and Transitional Cells.	Polymorphonuclear Neutrophile Cells.	Polymorphonuclear Eosinophile Cells.	Polymorphonuclear Basophile Cells.	Lymphocytes, Small and Large.	Large Mononuclear and Transitional Cells.
1.	Noon	8,000	63.7	1.1	0.6	31.3	3.3	5,100	90	45	2,500	265
	4 p.m.	10,400	65.6	0.9	0.6	26.0	7.0	6,825	95	60	2,700	730
2.	10 a.m.	7,000	55.0	2.7	0.8	36.2	5.5	3,850	190	50	2,535	285
3.	Noon	7,800	67.1	1.6	0.6	29.1	1.6	5,235	125	45	2,270	125
4.	Noon	13,500	64.8	2.0	0.3	30.3	2.6	8,750	270	40	4,100	350
	Noon	13,250	66.4	1.7	0.5	28.1	3.3	8,800	225	65	3,725	440
5.	Noon	7,000	60.5	2.7	—	31.7	5.1	4,235	190	—	2,220	355
6.	Noon	9,400	54.0	1.9	1.1	37.9	5.1	5,075	180	100	3,560	480
7.	Noon	9,600	57.9	0.3	—	35.8	6.0	5,560	30	—	3,435	575
8.	Noon	7,800	50.0	1.7	0.3	43.5	4.5	3,900	130	25	3,400	350
	2 p.m.	12,000	58.3	0.9	0.1	36.7	4.0	7,000	110	10	4,400	480
9.	8.30 a.m.	6,300	69.8	0.3	0.7	26.2	3.0	4,400	20	45	1,650	190
	10 p.m.	7,000	58.3	0.8	0.4	35.5	5.0	4,080	55	30	2,485	350
10.	4 p.m.	9,750	63.9	0.9	0.3	31.2	3.7	6,220	90	30	3,040	360
11.	5 p.m.	9,650	38.2	1.6	0.3	54.8	5.1	3,690	150	30	5,300	490
12.	5 p.m.	9,850	64.7	3.2	0.5	28.7	3.0	6,375	315	50	2,825	300
13.	5 p.m.	11,600	60.0	1.0	0.3	36.0	2.7	6,960	115	35	4,175	310
14.	5 p.m.	11,800	48.3	0.9	—	46.6	4.2	5,700	100	—	5,500	500
	5 p.m.	11,700	42.6	0.7	0.3	51.7	4.7	5,000	80	35	6,050	550
15.	3 p.m.	8,000	50.0	2.2	0.5	42.0	5.4	4,000	175	40	3,360	420

TABLE III.—PERCENTAGE AND ABSOLUTE NUMBERS OF LEUCOCYTE COUNTS ON INDIVIDUAL CASES.—*Continued.*

Males.

Number of Case.	Time of Day.	Total Count.	Percentage.					Total Number of Cells Per Cubic Millimetre.				
			Polymorphonuclear Neutrophile Cells.	Polymorphonuclear Eosinophile Cells.	Polymorphonuclear Basophile Cells.	Lymphocytes, Small and Large.	Large Mononuclear and Transitional Cells.	Polymorphonuclear Neutrophile Cells.	Polymorphonuclear Eosinophile Cells.	Polymorphonuclear Basophile Cells.	Lymphocytes, Small and Large.	Large Mononuclear and Transitional Cells.
16.	Noon	9,500	58.3	1.6	0.5	36.4	3.2	5,540	150	50	3,460	300
	5 p.m.	8,000	37.5	0.8	0.6	58.2	2.9	3,000	64	50	4,660	230
17.	11 a.m.	7,250	56.0	1.0	0.4	38.5	4.1	4,050	70	30	2,800	300
18.	Noon	6,650	50.7	2.2	0.3	41.8	5.0	3,370	145	20	2,780	335
19.	1 p.m.	9,750	41.6	2.0	0.7	49.7	6.0	4,050	195	70	4,850	585
	5 p.m.	12,000	37.1	3.3	0.4	52.9	6.3	4,450	400	50	6,350	750
20.	11 a.m.	6,000	50.7	1.0	0.3	42.5	5.5	3,050	60	20	2,550	330
21.	1 p.m.	7,800	41.7	2.3	1.0	51.0	4.0	3,250	180	80	3,980	310
22.	1 p.m.	7,600	55.5	1.0	0.3	40.3	2.8	4,220	75	25	3,065	215
23.	11 a.m.	5,250	48.3	0.7	0.3	46.8	3.8	2,525	35	15	2,450	200
24.	7 p.m.	12,200	52.6	1.9	0.2	39.9	5.4	6,420	230	25	4,850	660
25.	5 p.m.	7,000	37.0	1.3	0.5	55.5	5.7	2,600	90	35	3,885	400
26.	5 p.m.	8,150	50.8	1.0	0.2	42.8	5.2	4,140	80	15	3,500	425
27.	2 p.m.	10,700	61.4	1.4	0.3	30.9	6.0	6,570	150	30	3,300	640
28.	7 p.m.	9,600	57.1	1.4	0.3	37.2	4.0	5,480	135	30	3,570	385
29.	7 p.m.	8,400	64.3	1.1	0.3	30.4	3.9	5,400	90	25	2,550	330

mal limits, the majority having less than 0.5% and 50 cells per cubic millimetre, while 100 cells per cubic millimetre were not exceeded.

About three-fourths of these counts showed a lymphocyte content between 25% and 45%, the remainder varying between 45% and 60%.

Only two females had more than 4,500 of these cells per cubic millimetre, while in three of the males this count was exceeded. In two cases more than 6,000 lymphocytes per cubic millimetre were present. In the normal adult the lymphocyte count probably may vary from 15% to 60% and from 1,000 to 7,000 cells per cubic millimetre.

A correlation between lymphocyte and eosinophile counts has often been commented on and, though there is no such finding throughout this series, yet it is interesting to note that the individual with the highest lymphocyte count (6,350) also had the highest eosinophile count (400), while the one with the smallest lymphocyte count (1,650) showed the lowest eosinophile count (20 per cubic millimetre).

The endothelial leucocytes also showed a great range of normal variation in their relative and absolute numbers. The average count of these cells (4.5%) agrees closely with McJunkin's[1] figures (5.0%), obtained in the investigation of these endothelial leucocytes in thirty-four apparently normal people.

His special stain for these cells greatly facilitates their recognition.

Forty counts of the blood of twenty-nine normal individuals showed that in four total counts (three persons) the leucocytes fell between 5,000 and 6,000 per cubic millimetre; in twenty-six counts the leucocytes were between 6,000 and 10,000 per cubic millimetre; in eight counts the leucocytes were between 10,000 and 12,500 per cubic millimetre; in two counts (one person) the leucocytes were 13,250 and 13,500 respectively.

The physiological variation of the total leucocyte count in normal adults is probably between 4,500 and 15,000 leucocytes per cubic millimetre.

All these figures suffice to show that it is the range of variation of the normal leucocyte count and not the average count that is important. There is ample proof that a high percentage of lymphocytes is commonly found in the blood of normal adults. The tendency to attach undue importance to a fairly high lymphocyte count in the blood is a common error. Where this high lymphocyte count is the only apparent abnormality, no conclusion of any value can be deduced from the blood examination, unless it is found that the lymphocyte count constantly exceeds in absolute values the upper normal limit for the community. In many blood examinations the important point is not so much the total or percentage number of the various cells present, but the detection of certain pathological cell forms. It is the cell type that is likely to be the determining factor in diagnosis.

The impossibility of making a diagnosis in a difficult case on the findings of one blood examination alone cannot be too strongly emphasized. Several examinations are often necessary before the story of a blood disease can be pieced together. Even *post mortem* findings sometimes do not abolish the difficulty of making an accurate diagnosis in certain obscure blood conditions.

The examinations in Table IV. show that in the normal individual responding to the subcutaneous inoculation of a stock typhoid-paratyphoid vaccine, there is probably a depression of the activity of the bone marrow with regard to the production of the neutrophile leucocytes analagous to that which occurs in an enteric infection. It is unlikely that this alteration of the blood formula is due merely to a redistribution of the leucocytes, leading to the polymorpho-nuclear neutrophile cells being increased in

the internal organs and diminished in the peripheral circulation, for the reaction is present over a period of several days at least.

It is seen that in the seventeen examinations made while the patient was under the influence of the vaccine (from December 12 to 20, 1922), the polymorpho-nuclear neutrophile count was well below and the lymphocyte count somewhat above the average counts of these cells in this person at other times. The blood cell formula thus resembles in a general way the blood picture of typhoid fever.

Since making these observations, I have found that this question of the reaction of the blood cells to anti-typhoid inoculations was studied particularly in Germany during the war with results similar to those given above. There is a general agreement that each injection is followed by a leucopenia (Glinchikoff,[16] Courmont and Rochaix[17]).

THE LEUCOCYTES IN DISEASE.

The leucocytic response to disease may be roughly divided into two classes, though overlapping occurs:

(*i.*) With no pathological immature leucocytes in the circulating blood.

(*ii.*) With pathological immature leucocytes present in the blood.

1. The leucocytic response in the first class varies with the type of tissue infected, the clinical course of the disease and the infecting organism. Audain[6] states that where infection occurs in a tissue poor in lymphoid cells, the response will be mainly polymorpho-nuclear, whereas, even with the same organism at work, if the infection is in a tissue rich in lymphocytes, the latter will predominate. An acute infection often means a polymorpho-nuclear response, a chronic infection a lymphocytic one. As a general, though by no means invariable rule, there is a polymorpho-nuclear neutrophilic response to coccal infections, an eosinophilic response to helminthic infestation, a lymphocytic response to bacillary infection and a reaction on the part of the endothelial leucocytes in the case of protozoal invasion (as in malaria).

Leucopenia occurs in certain uncomplicated infections (typhoid, tuberculosis) where there is a depression of the activity of the red bone marrow. Severe infections with organisms which usually produce a stimulation of the bone marrow, may result in a paralysis of the cytoplastic activity of the red marrow with resulting leucopenia. A patient with acute miliary tuberculosis and a streptococcal empyema supervening on a *Bacillus typhous* infection

TABLE IV.—NORMAL INDIVIDUAL BEFORE AND AFTER TYPHOID INOCULATION.
The patient received the usual typhoid-paratyphoid vaccine against typhoid infections in January, 1921.

Date.	Time of Day.	Total Count.	Percentage.					Total Number of Cells Per Cubic Millimetre.				
			Polymorpho-nuclear Neutrophile Cells.	Polymorpho-nuclear Eosinophile Cells.	Polymorpho-nuclear Basophile Cells.	Lymphocytes, Small and Large.	Large Mononuclear and Transitional Cells.	Polymorpho-nuclear Neutrophile Cells.	Polymorpho-nuclear Eosinophile Cells.	Polymorpho-nuclear Basophile Cells.	Lymphocytes, Small and Large.	Large Mononuclear and Transitional Cells.
3.10.22	5 p.m.	8,000	37.5	0.8	0.6	58.2	2.9	3,000	64	50	4,660	230
12.10.22	Noon	9,500	58.3	1.6	0.5	36.4	3.2	5,540	150	50	3,460	300
9.12.22	——[1]	—	—	—	—	—	—	—	—	—	—	—
12.12.22	4 p.m.	7,800	43.2	2.2	0.6	46.0	8.0	3,370	170	50	3,600	625
16.12.22	——[2]	—	—	—	—	—	—	—	—	—	—	—
18.12.22	10 p.m.	9,300	34.1	1.9	0.1	57.5	6.4	3,170	175	10	5,350	600
20.12.22	7.30 a.m.	7,800	32.2	1.1	0.1	62.4	4.2	2,510	85	8	4,870	325
	9 a.m.	9,000	42.0	2.0	0.2	51.8	4.0	3,780	180	20	4,660	360
	10 a.m.	6,100	39.5	1.8	0.3	54.3	4.0	2,410	110	20	3,300	250
	11 a.m.	5,900	36.6	1.7	0.6	57.0	4.1	2,160	100	35	3,375	240
	Noon	8,400	41.0	1.7	0.4	53.0	3.9	3,450	130	35	4,450	330
	1 p.m.	9,200	34.6	1.9	0.9	59.0	3.6	3,185	175	85	5,430	330
	2 p.m.	7,000	37.4	2.0	—	57.4	3.2	2,620	140	—	4,000	225
	3 p.m.	6,600	34.3	3.0	0.2	58.8	3.7	2,275	200	13	3,880	245
	4 p.m.	8,400	34.7	1.2	0.3	59.8	4.0	2,915	100	25	5,000	335
	5 p.m.	8,500	31.6	1.6	0.8	61.6	4.4	2,700	135	70	5,235	375
	6 p.m.	7,500	40.0	1.5	0.3	54.0	4.2	3,000	110	20	4,050	315
	7 p.m.	7,100	36.5	1.2	0.7	56.1	5.5	2,600	85	50	4,000	390
	8 p.m.	8,400	38.5	2.0	0.5	54.8	4.2	3,230	170	40	4,600	350
	9 p.m.	6,500	30.2	1.0	0.2	65.0	3.6	1,965	65	13	4,225	235
	10 p.m.	7,400	31.8	1.7	0.5	63.2	2.8	2,350	125	35	4,575	210
22. 3.23	3 p.m.	9,600	49.0	2.2	0.4	44.4	4.0	4,700	210	40	4,260	385
Average before and after vaccine ..		9,000	48.3	1.5	0.5	46.3	3.4	4,350	135	45	4,170	300
Average during vaccine administration..		7,700	36.4	1.7	0.4	57.2	4.3	2,800	130	30	4,400	340

[1] On December 9, 1922, 500 million *Bacillus typhosus*, 250 millions each of *Bacillus paratyphosus A et B* given subcutaneously.
[2] On December 16, 1922, double the above dose was given subcutaneously.

had a leucocyte count of eight cells per cubic millimetre a few days before her death.

2. The abnormal leucocytes which may appear in the peripheral blood, are the immature forms of the various white blood corpuscles. Unfortunately our knowledge of the development of the leucocytes is very incomplete.

That the large mononuclear and transitional cells probably arise from the endothelial lining of special areas of the blood vascular system is strongly suggested by the experimental work of Aschoff and Kujono[7] and of McJunkin[8] and the embryological investigations of Florence Sabin[9] and numerous other workers. These cells are probably identical with the clasmatocytes of connective tissue.

Lymphocytes may occur wherever there is a reticulum, as in lymph glands, spleen, bone marrow and various other organs. They are probably formed from the cells of the reticulum and sinus endothelium in these various situations.

The vast majority of the granular leucocytes arise in the normal individual in the red bone marrow, which is also the most obvious site of production of the red blood corpuscles. The granular leucocytes have an inevitable association with changes in the red cell content of the blood.

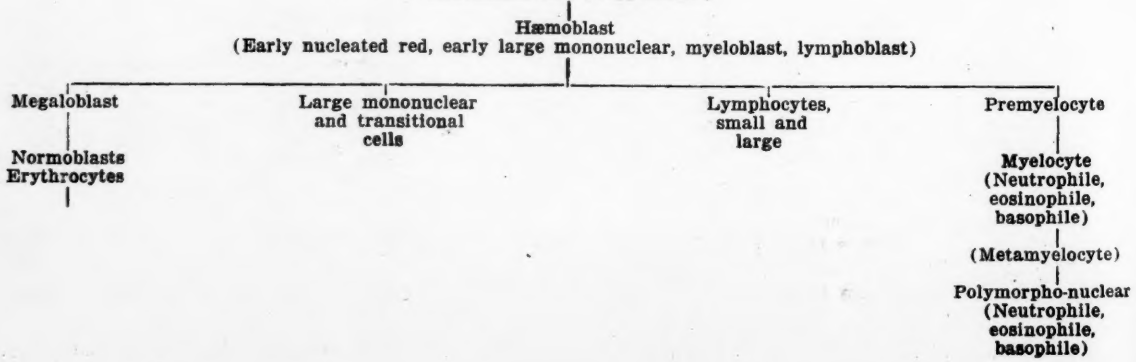
In the fœtus blood formation in the embryo is at first obviously diffuse, later becoming localized more particularly in the liver, the spleen and finally in the bone marrow. This is the accepted teaching of the present day, but Pappenheim's[10] last work will probably lead to some modification of our ideas on this subject. His conception is that the cells giving rise to the blood corpuscles have the form of the endothelial lining of a capillary, arterial, venous or lymphatic. Stimuli reaching certain of these cells by the blood or lymph cause them to divide, giving rise to the immature forms of the various leucocytes and red blood cells which, when they become mature, make their way into the circulation. Pappenheim holds that there is only one blood-forming organ, the reticulo-endothelial system, which pervades the whole body and is localized chiefly in the lymphatic glands, the spleen, the hepatic capillary system and the bone marrow capillaries, the usual sites of blood cell formation in the fœtus. The bone marrow merely shows in a conspicuous manner the processes which may occur in any capillary in the body. The blood-forming tissues (myeloid, lymphatic and erythroblastic) are thus diffuse throughout the body. Such a conception of the origin of the blood corpuscles simplifies many of the problems of leuchæmia and allied diseases.

When an investigation of the abnormal cells of the blood is made, it is found with ordinary staining methods to be practically impossible to differentiate between the early cells of the red and white series. The argument in the acute leuchæmias as to the differentiation between the lymphoblast and the myeloblast still continues. The most primitive pathological white cells (so-called hæmoblasts) appearing in the blood are invariably distinguished by the company they keep, being classed as myeloblasts if the predominating cell is a myelocyte, lymphoblasts if the predominant cell is a lymphocyte. From their morphological characters alone it is impossible to distinguish them.

Diagrammatically the evolution of the abnormal cells occurring in the blood may be illustrated as in the graph.

The only abnormal forms which concern us at present, are the hæmoblasts, the premyelocytes and the myelocytes. Nothing is gained by an undue multiplication of the stages of development of these various cells, the only result being such a multiplicity of names that the student is lost in a maze of useless terminology. Naturally the transition stages are not abrupt, perhaps ten or twenty divisions of the premyelocyte occurring before the typical myelocyte is produced and numerous intermediate forms will therefore occur at any stage of the evolution of the cell.

As a general rule the more immature the white cell is, the more foamy and fragile and the more basic (*id est*, the more intense deep blue with ordinary stains such as Leishman's) is its cytoplasm, the more active looking is its nucleus and the larger is the nucleus in proportion to the rest of the cell. Hence the hæmoblast is a cell usually about the size of or a little larger than a polymorpho-nuclear leucocyte with a large, round or oval, central or eccentric, fairly deeply staining nucleus with several nucleoli, the nucleus occupying the greater part



of the cell and being definitely marked off from a cell body irregular in form with fragile, foamy, non-granular cytoplasm staining an intense deep blue with ordinary stains.

The various oxidase staining reactions fail to help in determining the type of cell to be derived from this hæmoblast. This cell is occasionally found in the circulating blood and it is only from a careful study of the types of cell with which it is associated, that any conclusion as to its place in the evolution of any particular type of leucocyte can be formed. Its presence in the blood indicates a very intense stimulation of the hæmopoietic system with very vigorous production of the cell type dominating the blood picture. This cell is difficult to distinguish from the large lymphocyte, but the latter has lighter staining cytoplasm and a darker nucleus, with coarse, irregular bands of chromatin and fewer nucleoli.

The premyelocyte is the earliest definitely recognizable cell of the granular series of leucocytes. It is larger than the hæmoblast, often being about 16 μ to 20 μ in diameter. The cytoplasm is still foamy and fragile, but stains a less intense blue than in the hæmoblast. A good polychrome stain shows beginning fine granulation in the blue cytoplasm. The nucleus is still large relatively to the rest of the cell, is round or oval, central or eccentric, closely skeined and not so deeply staining as the nucleus of the hæmoblast. Several nucleoli may be present. The nucleus is sharply marked off from the cytoplasm.

The premyelocytes, on the one hand, approach closely to the hæmoblasts and on the other to the myelocytes, there being naturally a gradual transition from the one series to the other. More information regarding these early cells of the granular series is obtained with a good polychrome stain than with any of the oxidase staining reactions. The appearance of these cells in the blood stream indicates a very intense stimulation of the myeloid formative tissues of the hæmopoietic system.

The neutrophile myelocytes vary in size from that of a red blood corpuscle up to that of a large mononuclear cell, the smallest and largest types being found only in myelogenous leuchæmia. Usually they are from 12 μ to 16 μ in diameter. The cytoplasm has lost the deep blue staining of the earlier forms and contains numerous neutrophile granules which do not stain as well as those of the mature leucocyte. The nucleus is relatively large, occupying at least half of the cell, and is usually central and round or slightly indented. The nucleus does not stain deeply, so there is no sharp differentiation of nucleus from cytoplasm. Transition forms again occur towards the premyelocytes on the one hand and the mature leucocytes on the other. As the cell approaches maturity the nucleus becomes more indented and more pyknotic. This intermediate form between the polymorpho-nuclear leucocyte and the myelocyte is sometimes termed the metamyelocyte, but, as stated before, an undue multiplication of the stages of evolution of the leucocytes only tends to confusion.

As uniformity of diagnosis of these various types of cell is essential, it is well to regard with Emerson[11] all granular cells with faintly staining, round, oval or kidney shaped nuclei as myelocytes, provided that the nucleus occupies at least half of the cell, while a cell with a more compact, more distorted, more definitely stained and relatively smaller nucleus is classed with the leucocytes. The nucleus of some leucocytes is round or oval, occupies only a small portion (say, a fourth) of the cell and stains deeply and diffusely. Such cells on side view would show the polymorphous character of the nucleus.

The eosinophile myelocyte is likewise a large cell, usually varying from 10 μ to 16 μ in diameter, with a pale, round or indented nucleus and comparatively scanty cytoplasm containing the characteristic eosinophile granules. Again transition stages to the mature eosinophile leucocyte may be seen.

The basophile myelocytes are somewhat similar cells, distinguished by the characteristic irregular shaped basophilic granules in their cytoplasm.

All observers agree that the red bone marrow is the most important blood-forming tissue in the body. Yet, as Piney[12] has shown, most text-books of hæmatology are misleading, even with regard to the macroscopic anatomy of the normal red marrow at the various ages. Microscopic examination of the red marrow shows all the immature forms of red and white blood corpuscles enumerated above, the neutrophile myelocytes predominating. Giant cells are also present.

Occasionally red marrow of typical cellular structure is noted in the normal adult in situations other than the medullary cavities of bones. It has been observed in the pelvis of the kidney in a normal adult male, but is more frequently seen in leuchæmia.[13]

Little as is our knowledge of the formation of the white blood corpuscles, our knowledge of the normal processes of their destruction is even less.

THE LEUCHÆMIAS.

The leuchæmias show more distinctly than any other diseases the presence of pathological immature cells in the circulating blood.

The following analysis of forty-one patients with leuchæmia admitted to the wards of the Melbourne Hospital in the last thirteen years will show the more important clinical aspects of this disease.

The following classification was adopted: (*a*) Acute leuchæmia, eleven (including one patient with possible chloroma; (*b*) chronic myeloid leuchæmia, twenty-five. (*c*) chronic lymphatic leuchæmia, five.

All statistics show the preponderance of this disease in males and here the proportion of males to females was about five to two.

The types fall roughly into different age periods—youth, middle and old age. Nearly three-fourths of the patients with acute leuchæmia were between the ages of fifteen and thirty-one years (patients under fourteen years are not admitted to this Hospital). The eldest of these patients was fifty-six years old.

The age of election for chronic myeloid leuchæmia is between thirty and fifty years. Over 70% of these patients were within this age period.

The youngest patient was twenty-eight, the eldest

seventy-three years of age. Only two patients were over sixty years old.

In the chronic lymphatic group two patients suffered rather from a subacute type of the disease, dying six to nine months respectively after the onset of symptoms. Both were under thirty-five years of age.

Two of the three whose type of disease conformed more closely to the recognized chronic type, were over sixty years old.

This peculiar age incidence of the various types of this disease is probably related to the normal changes which occur in the red marrow during life. As Piney[12] has shown, from infancy to old age there is normally a progressive diminution in the amount of cellular marrow in the limb bones and a progressive increase in the amount of fat. In advanced old age no red marrow may be detected in the epiphyses and even the diaphyseal patch may have almost completely disappeared. This absolute diminution in the amount of the red marrow, together with the decreasing ability to react to stimuli which the red marrow will share with the other tissues in advanced age, may explain the low leucocyte counts often noted in leuchæmia in old people, as well as the change in type of leuchæmia at the various age periods. In infections and in new growths important modifying factors are introduced by the type of tissue attacked and the degree of reaction of that tissue. So in leuchæmia the reaction of the affected tissue is probably as important as the primary causative agent. In old age how often is a pneumococcal infection associated with a poor leucocytic response when compared with the almost invariable high leucocytosis shown in these circumstances by the healthy young adult?

Predisposing Causes.

Trauma and infection did not occur sufficiently frequently to suggest anything more than coincidence. Pyorrhœa was frequently observed, as it is in the majority of hospital patients. Free hydrochloric acid was absent from the gastric juice of the only two patients (both with chronic myeloid leuchæmia) whose gastric contents were examined, being probably secondary to the definite anæmia (red corpuscles, 3,500,000) which was present in both patients at this time.

Acute Leuchæmia.

The dividing line of acute from chronic leuchæmia is often not well defined, an acute exacerbation of a chronic leuchæmia often simulating a primary acute leuchæmia.

In this series the duration from apparent onset to death varied between one and three months in all but one patient whose illness lasted four and a half months. The patients invariably died within a month of admission to hospital.

The onset is usually fairly acute, the first symptoms noted most frequently being malaise, headache and sore throat. One patient complained first of pain resulting from trauma to the lower end of the tibia, followed in a few weeks by pain and tenderness over the lower ends of both ulnæ. Ten weeks after the initial accident the patient died. The acute onset, with headache, malaise and high fever which was invariably present, frequently suggested an ordinary acute infection and the disease was often overlooked.

Malaise and prostration were marked in every case. Hæmorrhages were noted in all but one patient whose record is very incomplete. Epistaxis, bleeding from the swollen, spongy gums, subconjunctival hæmorrhages and petechial or purpuric extravasations were most common. Retinal hæmorrhages were present in the only patient submitted to ophthalmoscopic examination.

Bleeding from the stomach and bowel were not commonly observed, while hæmaturia was noted only once. Metrorrhagia was the first indication of trouble in one of the two females in this group, the uterus being curetted before the correct diagnosis was made.

Gastro-intestinal symptoms, vomiting, constipation or diarrhœa were present in half the cases at some stage, while dyspnœa, secondary to the marked anæmia, was noted in the same number. Abdominal pain and loss of weight were rarely complained of. Sweating was not observed, though a rigor occurred in two patients. Pallor was marked in every patient.

Fever was invariable; it was usually remittent, sometimes continuous, rarely intermittent; sometimes as high as 40° C. (104° F.), but more frequently about 39° C. (102.2° F.).

Tenderness over the bones (especially the sternum and ribs) was present in two patients.

The spleen was palpable in eight of the eleven patients, being definitely enlarged in three, though in none did it reach quite to the umbilicus.

The liver was palpable in half the patients, usually about one finger's breadth below the costal margin.

Some glands, external or internal, were enlarged in every patient but one, the cervical glands being palpable in eight, the axillary glands in seven, the inguinal glands in five, while necropsy revealed enlarged mediastinal or abdominal glands in four of the five patients examined.

The clinical picture of the disease, then, is that of an acute infection with hæmorrhages, high fever and prostration, usually associated with some enlargement of spleen and cervical lymph glands. The pallor and the swollen, spongy, bleeding gums suggest a blood examination and, as in the early stages the total count is often sub-leuchæmic, a differential count will be required to determine the diagnosis.

The Blood Examination.

A marked progressive anæmia usually developes rapidly. The red cell count in the patients examined varied between 725,000 and 5,500,000 per cubic millimetre.

In eight patients the number of red cells did not exceed 3,000,000 and at some stage was less than 2,000,000 per cubic millimetre.

Nucleated red blood corpuscles (normoblasts and megalobasts) were usually present, with alteration in size and shape of the red blood corpuscles.

The colour index was usually about 0.9, 0.65 being the lowest recorded.

At the onset the white cell count is practically always sub-leuchæmic, ranging from a few thousand to 30,000 per cubic millimetre. A few are aleuchæmic throughout. The high figures of chronic myelogenous leuchæmia are rarely reached.

The first count made of the blood cells of four of these patients showed the total white count to be under 30,000, the lowest being 13,000 per cubic millimetre. In only four patients did the total number exceed 100,000 during the course of the disease, the highest recorded being 500,000 leucocytes per cubic millimetre.

The films invariably showed a preponderance of the cells typically seen in these cases and described previously under the names of hæmoblasts and premyelocytes. In addition, myelocytes were usually present, while in some there was a fair proportion of small lymphocytes. Eosinophile or basophile cells may be absent, while neutrophile leucocytes may be scarce. Occasionally the myeloblasts are of small size, resembling the small lymphocyte of chronic lymphatic leuchæmia.

Diagnosis.

Though it is usually taught that there are two types of acute leuchæmia, the myeloblastic and the lymphatic, the modern tendency is to relegate the latter further and further into the background.

Clinically no distinction can be drawn between the two types and the diagnosis is usually based on certain fine distinctions in the primitive cell type present. In the so-called acute lymphatic leuchæmias myelocytes are rarely seen, though a stimulation myelocytosis may cause them temporarily to appear in the blood to as high a figure as 10%.

In the aleuchæmic and sub-leuchæmic stages a careful differential count is essential to confirm the diagnosis. Ordway and Gorham[13] state that a diagnosis of acute leuchæmia to avoid criticism should show an aleuchæmic or sub-leuchæmic stage (total count under 30,000) a progressively downward trend to death usually in less than four months, the typical blood picture—myeloblasts, premyelocytes and myelocytes in the acute myelogenous leuchæmia and a preponderance of abnormal "lymphocytic" types, with few myelocytes in so-called lymphatic leuchæmia—and the typical macroscopic and microscopic lesions in liver, spleen, lymph glands and bone marrow.

Differential Diagnosis.

The diagnosis of a hyperleucocytosis from a leuchæmia is often very difficult, while time is the main factor which makes obvious the distinction between acute infective lymphoblastosis and leuchæmia. Both these difficulties will be considered later.

Another difficulty sometimes is to distinguish between a primary acute leuchæmia and an acute leuchæmia supervening on a latent chronic leuchæmia. A careful clinical history will render this difficulty negligible in most cases.

Clinically, as is suggested by Ordway and Gorham,[14] several types of this disease may be found.

(*i.*) With severe ulcerative and gangrenous processes in the mouth, little hæmorrhagic tendency and little enlargement of spleen or lymph glands. This type is illustrated in this series by a female who was first sent to the Infectious Diseases Hospital at Fairfield as probably suffering from diphtheria.

(*ii.*) With the hæmorrhagic tendency the dominant feature of the case. The condition of one patient with persistent metrorrhagia was considered to be abortion and curettage of the uterus was done.

(*iii.*) Cases of less virulent type, in which swelling of the lymphatic gland and splenic enlargement are the salient features, as is illustrated in a case history recorded later.

(*iv.*) A type at first showing only fever and marked anæmia, but later conforming to one of the previous three types.

To these may be added type (*v*), with toxic features and slight enlargement of spleen and perhaps lymphatic glands. This condition is frequently mistaken for typhoid fever or acute ulcerative endocarditis and other septicæmic conditions. These faulty diagnoses were made in three of the patients in this series.

The differential diagnosis of any of these types of the disease from similar conditions depends on a careful blood examination.

Prognosis.

These patients all died within six weeks of admission to hospital, the longest time elapsing from the onset of the first symptoms till death in any case being four and a half months. Death was hastened in one patient by an infection with a gas-producing organism; in the others the fatal result was apparently due to the disease itself.

Pathology.

Five patients were examined *post mortem*. Hæmorrhages were present in every case but one.

The spleen is usually not greatly enlarged, the heaviest spleen being 900 grammes (two pounds), the others weighing between 225 and 340 grammes (eight and twelve ounces).

The liver also is not very large, 2.6 kilograms (92 ounces) being the weight of the largest specimen.

Glandular enlargement was variable in extent and degree, being present in every case but one, especially in the cervical region. A persistent thymus was observed in one patient, aged fifteen.

The grey or red bone marrow showed microscopically a preponderance of myelocytes, premyelocytes and myeloblasts at the expense of the red blood corpuscles.

The only certain evidence of acute leuchæmia is derived from histological study of the cell type undergoing hyperplasia in the tissues. Typically there is a diffuse hyperplasia of myeloid elements in the various organs, the myeloblast being the predominating cell type.

Chronic Myelogenous Leuchæmia.

This is a disease of insidious onset, progressing so quietly that in this series of cases the average duration of symptoms before medical advice was

sought was fourteen months, the extremes being four weeks and four years.

The first symptoms were due to one of two causes, splenomegaly or secondary anæmia.

In over 50% of the patients, the first complaint was either of swelling of or a lump in the abdomen (the enlarged spleen) or of pain over the region of the spleen. The secondary symptoms of a moderately severe anæmia, lassitude, weakness, dyspnœa and gastro-intestinal symptoms (vomiting and diarrhœa), were the other initial complaints.

Pain was the only symptom which brought the patient to a medical practitioner within a few weeks, otherwise months or years elapsed before advice was sought.

During the course of the disease the most prominent symptoms again were either those due to the enlarged spleen (swelling of the abdomen or pain over the enlarged spleen) or those due to the secondary anæmia (lassitude, weakness, pallor, wasting, cough, dyspnœa, œdema, anorexia, diarrhœa, vomiting, constipation). Of these the gastro-intestinal symptoms were the least frequent. The spleen in some cases was appreciably diminished in size after an attack of diarrhœa. This was sufficiently definite to be observed by two of the patients in this series.

Pallor was absent in only three of these patients, the red cell counts in these persons being 5,000,000, 3,750,000 and 2,500,000 per cubic millimetre respectively. The patient with the last named count was flushed and feverish.

Retinal hæmorrhages and hæmorrhages from the nose and bowel were fairly common in the later stages, bleeding from the gums and purpuric or petechial rashes were less frequently observed, while hæmorrhages in other situations were relatively uncommon.

Tenderness over the bones was found in only one patient.

Fever was present in nearly 90% of the patients during their short stay in hospital. Usually it was of mild degree (under 37.8° C. or 100° F.) and lasted only for a few days. In others the maximum temperature varied between 37.8° C. and 39.4° C. (100° F. and 103° F.).

Sweating and chills were rarely noticed.

Nervous symptoms are rare, being due either to hæmorrhage or to leuchæmic infiltration of the nervous tissue.

Despite any remissions, spontaneous or while under treatment, the gradual progress of the disease is shown by the increasing severity of the symptoms of the anæmia, the patient eventually becoming bedridden until death ensues from myocardial insufficiency (secondary to the anæmia), intercurrent infection or after a severe hæmorrhage.

On examination pallor and wasting were often very noticeable. The spleen was invariably much enlarged. In only two patients did it fail to reach as far as the umbilicus. In one-third of the patients it extended into the pelvis and across the mid-line of the abdomen. In one patient with a ptosed spleen which had twisted on its pedicle, the misplaced organ was mistaken for an ovarian cyst, as it seemed to rise out of the pelvis.

Occasionally a definite friction rub is audible over the enlarged spleen.

The liver was not palpable in one-fourth of the patients, while in an equal number it reached to the umbilicus. In the remainder it was felt between the costal margin and the umbilicus.

Slight enlargement of lymphatic glands was present in about half of these patients. In the early stages it is very rarely seen, though later in rare instances enlargements of considerable size may be found.

In the only two patients whose gastric contents were examined, free hydrochloric acid was absent, presumably secondary to the anæmia (3,500,000 red blood corpuscles per cubic millimetre) present in each case. These were examined by the old method, not by the more recent fractional method.

Ascites was present in two patients, one of whom was suffering from a syphilitic myocarditis as well as leuchæmia.

The basal metabolism[34] [35] is increased in both forms of leuchæmia, usually being 40% to 50% above normal, the intensity of the rise in basal metabolism being parallel with the clinical severity of the disease. This increased metabolism is probably due to the active metabolism of a large number of immature leucocytes. In the only patient in whom the basal metabolism was investigated, it was found to be 18.4% above normal.

Blood Examination.

In the early stages, anæmia is not severe, but by the time the patient usually comes for advice, a definite secondary anæmia is present. The lowest red cell count on being first seen was 2,000,000, the highest 5,000,000, the average 3,350,000. When first seen the anæmia was moderate (over 3,000,000) in 60%, severe in 40% (2,000,000 to 3,000,000).

The lowest red cell count in the series was 1,500,000 per cubic millimetre. The colour index was usually between 0.8 and 0.9. The fall in hæmoglobin and in the red cell count is gradual and progressive and the colour index is usually low.

Nucleated red blood corpuscles are invariably present, even when the anæmia is not marked.

The blood platelets are increased in number.

The lowest white cell count on admission was 40,000, the highest 1,000,000, the average 300,000. In over half the patients it was between 100,000 and 500,000, in one-fourth it reached from 500,000 to 1,000,000. The lowest white cell count while under observation was 8,000 cells per cubic millimetre.

The blood film is usually typical, the heterogenous collection of cells contrasting with the monotonous film of chronic lymphatic leuchæmia.

The film shows a preponderance of polymorphonuclear neutrophile leucocytes (30% to 80%) and myelocytes (20% to 40%), while eosinophile and basophile leucocytes and myelocytes are present in varying proportions. Premyelocytes and myeloblasts are usually to be seen in small numbers, while lymphocytes and large mononuclear cells are also present.

Three patients in this series showed a terminal acute leuchæmic condition supervening on the chronic disease, the films then showing a more monotonous character with a predominance of myeloblasts.

The diagnosis of this disease rests on an examination of the blood film, the large total numbers of myelocytes, eosinophile cells and mast cells, with the presence of nucleated red blood corpuscles, being the characteristic features.

Duration.

The eight patients who died while under observation, had noticed symptoms from six months to seven years (average twenty-two months) before death. The patient who died within six months, was suffering from syphilis as well as leuchæmia and died water-logged as the result of cardiac failure. The one who lived for seven years died from failure of the right side of the heart within a few hours of splenectomy. In another patient death was due to hæmorrhage and asthenia following the removal of several teeth. Three others died from intercurrent pneumonia. Cardiac failure and a terminal acute exacerbation of the leuchæmia were responsible for the remaining two deaths.

Prognosis.

The disease is invariably fatal, usually within two years of onset, though in many cases it exceeds this period. Secondary infection should be guarded against, for the immunity reactions in a leuchæmic patient are not normal. Great care should be taken in any operative procedure to prevent subsequent hæmorrhage with its debilitating effects.

Pathology.

Only five patients were examined *post mortem*. The characteristic lesions are found in the blood-forming organs, the other tissues showing macroscopically only the evidences of severe anæmia.

The spleen is often huge, extending right into the pelvis. The largest spleen in this series weighed 4.3 kilograms (nine and a half pounds), though the organ may be nearly twice this size in rare cases. The spleen is smooth and retains its normal shape. Perisplenitis is usually present. Infarcts were found in two cases. The cut surface is typically of a maroon colour.

The liver is often enlarged, the heaviest in this series weighing 6.25 kilograms (thirteen and three-quarter pounds). Slight glandular enlargement was noted in four of the five patients; it was rather evident in the abdominal glands of one patient.

The bone marrow was of greyish, granular appearance, the normal fat marrow having been replaced by cellular marrow. Microscopically it showed predominance of the early forms of granular leucocytes. The essential lesions, as Cabot[15] points out, are due to myeloid transformation of the spleen and of the lymphatic system with hyperplasia of the leucocytic elements of the bone marrow and intracapillary myeloid infiltration in the liver and to a less extent elsewhere through the body. Microscopically this myeloid transformation and infiltration is easily observed.

Chronic Lymphatic Leuchæmia.

In two of the five patients in this group the affection was rather subacute in type; both died within nine months of the onset of the disease. The typical chronic lymphatic leuchæmia usually lasts for some years.

The onset is very insidious and the disease is usually fairly well advanced when the patient is first seen. By this time anæmia is invariably present, so that pallor, weakness, lassitude, wasting, dyspnœa and œdema are the most frequent symptoms. Often the accidental discovery of painless enlargements of lymphatic glands may cause advice to be sought, while progressive enlargement of the abdomen or pain over the spleen may be noticed. Vomiting and diarrhœa are the most common gastro- intestinal symptoms.

Hæmorrhages occurred in all but one patient, a petechial or purpuric rash being most commonly observed.

Chills and sweats are rare. Irregular fever of slight degree (to 37.8° C. or 100° F.) is usually present at some stage of the disease.

The spleen is usually enlarged, reaching to the umbilicus in two patients and to the iliac crest in another.

The liver was obviously enlarged in only one patient.

The most constant physical finding is general extensive glandular swelling. The superficial glands were enlarged in all these patients, while in two there was evidence of enlargement of the mediastinal glands. The glands are firm, painless, discrete and freely movable, any matting together being due to secondary infection.

Cutaneous lesions of great variety are common in this disease, though none occurred in these few patients.

Blood Examination.

The average red cell content of the blood of these patients when first seen was 3,100,000. The red count falls progressively towards the end. The red cells varied between 900,000 and 4,250,000. Nucleated red blood corpuscles were not as common as in the cases of myelogenous leuchæmia.

The white cell count ranged from 300,000 to 3,200, both counts occurring in the same patient while under treatment. Perhaps over-energetic treatment resulted in a paralysis of the activity of the hæmopoietic organs. The patient died without any further leucocyte counts having been made.

Only two patients yielded counts exceeding 70,000 while under observation. Usually the white cells ranged between 20,000 and 50,000 per cubic millimetre.

This comparatively low count is quite common in chronic lymphatic leuchæmia.

Films showed from 80% to 97% of lymphocytes, mostly of the small variety. The patient who died six months after onset, showed in the later stages a fair proportion of larger immature forms. These patients frequently manifest remarkable remissions in the disease, sometimes spontaneously, sometimes while under treatment and sometimes as a result of an intercurrent infection.

Post mortem examination reveals generalized enlargement of the lymphatic glands, spleen and often of the liver. Microscopically the great lymphocytic infiltration of glands and spleen obscures the normal structure. In the liver, as with myelogenous leuchæmia, these cells are found in the sinusoids between the columns of liver cells and in the periportal spaces. Similar infiltration may occur in other organs. The normal fatty bone marrow is replaced by a dense cellular grey tissue showing microscopically the complete preponderance of lymphocytic cells over the normal myeloblastic and erythroblastic tissue.

Ordway and Gorham[14] point out that there is a remarkable tendency to accumulations of lymphocytic cells about blood vessels in the various tissues and this may be so marked beneath the endothelium of the smaller veins that occasionally actual loss of continuity of the endothelium results, so that these lymphocytes are potentially within the smaller veins. This appearance of invasion of the blood vessels by masses of lymphocytes suggests the possible explanation of the mode of transition from sub-leuchæmic to leuchæmic stages of leuchæmia and perhaps from lympho-sarcoma to leuco-sarcoma, as will be discussed later.

The Leuchæmias and Allied Conditions.

The leuchæmias are closely related on the one hand to the acute infections and on the other to new growths. Again an unnecessarily complex terminology has led to confusion. The term pseudo-leuchæmia has been applied to so many and diverse conditions since it was introduced by Cohnheim that it should be dispensed with. Most cases grouped under this heading are found with modern methods of investigation to be examples either of Hodgkin's disease or of aleuchæmic leuchæmia. So-called mixed leuchæmias do not occur, the origin of this term being the old difficulty of distinguishing between the myeloblastic and the lymphocytic cells. Similarly the term leuchanæmia should be dropped, such cases belonging either to the leuchæmias or the severe anæmias.

The diseases closely related to leuchæmia may be classified as follows:

(*i.*) Hyperleucocytosis occurring in response to definite infection.
(*ii.*) Acute infective lymphoblastosis (or lymphomatosis or mononucleosis).
(*iii.*) Leuchæmias, leuchæmic and aleuchæmic.
(*iv.*) Leuco-sarcoma (Stærnberg).
(*v.*) Chloroma.
(*vi.*) Lympho-sarcoma (local and general).
(*vii.*) Hodgkin's disease.

Hyperleucocytosis in Response to Definite Infection.

Throughout the literature of blood diseases cases of excessive leucocytosis associated with definite acute infection are frequently recorded. Cabot,[15] Stevens,[18] Austrian,[19] Hirschfeld and Kothe[20] among others report cases of infection in children (pertussis, pneumonia, mastoiditis, appendicitis) giving rise to an unusually great increase in the white blood corpuscles, as well as the appearance of abnormal immature leucocytes in the blood.

Bourne and Scott[21] report a case of pertussis with broncho-pneumonia in an infant showing a count of 176,000 leucocytes per cubic millimetre, of which 116,000 were lymphocytes. Reiche[22] reports a case of whooping cough combined with influenza in which the total white count was 172,000 per cubic millimetre. Blatteis[42] reports the case of a man, forty-five years old, just recovering from influenza, who showed a leucocyte count of 100,000 per cubic millimetre, myelocytes being 48% and eosinophile cells 10% to 14%. The liver and spleen were enlarged. The blood count soon returned to normal and the symptoms cleared.

In this connexion the following case history is very interesting:

C.B., male, aged forty-seven years, labourer, was admitted to hospital on July 24, 1922, with the provisional diagnosis of left lobar pneumonia.

He had suffered from pneumonia some years previously, but otherwise until this illness he had been quite healthy. The family history was clear. The present illness began on July 3, 1922, three weeks prior to admission to hospital, with pain in the foot which later moved to the shoulder and finally settled in the left axilla. At this stage he took to bed. No rigor had occurred. The doctor in attendance diagnosed pneumonia. A week later the patient was allowed up, but for the next ten days he felt "off colour" and spent much of the time in bed. Four days before admission on July 20, 1922, pain again commenced suddenly in the left axilla. There was no rigor. Cough with whitish sputum was present. The bowels were constipated.

On examination on July 24, 1922, the patient looked very ill and pallor was very distinct. The temperature was 38.5° C. (101.4° F.), the pulse rate 132, regular, the respirations 40 and the systolic blood pressure 100 millimetres of mercury. The tongue was dry and coated. The urine contained albumin and granular casts. There was dulness at the base of the left lung, where tubular breathing and coarse, crackling crepitations were easily heard. The rest of the examination failed to elicit anything noteworthy.

On July 27, 1922, the patient was obviously worse, with marked pallor, offensive breath and distended abdomen. Little urine was being passed. It was loaded with casts and contained some pus cells and coliform organisms.

There was a slight epistaxis.

Examination of the chest showed the typical physical signs given by fluid in the pleural cavity.

The chest was needled without result. The temperature since admission had been of the remittent type, varying between 38.3° C. and 39.4° C. (101° F. and 103° F.).

At midnight the patient was obviously worse. The chest was again explored without result. The abdomen was distended. There was no palpable enlargement of the liver, spleen or lymphatic glands. That night the patient died after being ill for twenty-four days.

Blood examination four hours before death showed:

Red blood corpuscles	3,800,000 per cubic millimetre
Hæmoglobin (Tallqvist)	80% (?)
Leucocytes	277,000 per cubic millimetre

The differential count was as follows (2,000 cells having been counted):

Polymorpho-nuclear neutrophile leucocytes	3.0% =	8,300 per c.mm.
Neutrophile myelocytes	78.9% =	218,550 per c.mm.
Premyelocytic forms	2.1% =	5,820 per c.mm.
Large lymphocytic forms	4.3% =	11,900 per c.mm.
Small lymphocytic forms	12.0% =	33,250 per c.mm.
Normoblasts	0.5% =	1,385 } 3,600 per
Megaloblasts	0.8% =	2,216 } c.mm.

The films showed definite though comparatively slight poikilocytosis and anisocytosis, the larger forms being fairly frequent, the smaller cells infrequent. Polychromasia and basophilic stippling were present, though not very noticeable.

The vast majority of the leucocytes in the film were typical neutrophile myelocytes. Mature polymorphonuclear neutrophile leucocytes were rarely seen, most of

the cells in this class being rather late stages of the so-called metamyelocytes. It is highly probable that a large proportion of the so-called lymphocytic forms, large and small, belong to the myeloblast group.

The notable absence of eosinophile cells and mast cells is highly suggestive that in this patient there was a toxin with a special affinity for the neutrophile leucocytes and that the response was a final desperate effort on the part of the bone marrow to deal with the victorious invaders. The differential count is unlike that usually seen in either a chronic or an acute leuchæmia, while the history of the illness is definitely of short duration and does not resemble the usual clinical history of acute leuchæmia.

Necropsy revealed some toxic spoiling of an otherwise apparently normal heart. The right lung was somewhat emphysematous. The upper lobe of the left lung was completely collapsed, owing to the left pleural cavity being full of oily stinking pus. The lower lobe was consolidated, having the appearance of lobar pneumonia at the end of the stage of red hepatization. The lower portion of the upper lobe showed a small area of consolidation. Numerous adhesions were present in the left side of the chest, while a few old adhesions were noted in the right pleural cavity.

The spleen had the typical soft, mushy appearance seen in any septicæmic condition. It was only slightly enlarged. The liver and kidneys likewise showed evidence of toxic spoiling. The glands were not obviously enlarged in any situation. Lung culture *post mortem* did not lead to the growth of any bacteria. From the sputum shortly before death a Type III. pneumococcus was isolated. Unfortunately the pus in the pleura was not cultured.

Macroscopically the *post mortem* appearances did not resemble those of leuchæmia.

Microscopically the lung showed the typical appearances of lobar pneumonia at the stage of transition from red to grey hepatization.

Section of a lymph gland showed a fair degree of vascular dilatation with sinuses distended with mononuclear cells. The endothelial cells of the sinuses and the reticulum showed great activity, with marked increase in the number of flattened endothelial cells. Giant cells were present in small numbers. Lymph follicles were well marked. The picture rather suggests a chronic inflammatory condition.

In the liver columns of liver cells showing some degree of toxic spoiling were separated by dilated sinusoids containing red blood corpuscles and an excess of leucocytic cells, mainly mononuclear. In the periportal zones there were accumulations of apparently identical mononuclear cells. Pigmentation of the cells of the centre of each lobule was noticeable. The connective tissue of the liver was not increased. The picture resembles that of a mild myelogenous leuchæmia.

The spleen showed sinuses and blood vessels dilated and packed with red blood corpuscles and myelocytic cells. The Malpighian bodies were not easily recognized, while many cells of more varied types than usual were present throughout the splenic pulp, the histological picture closely resembling that of myelogenous leuchæmia.

The resemblance to myelogenous leuchæmia was also noted in the kidney, where in a few areas there were accumulations of cells similar to those in the liver. In addition, cloudy swelling and fibrosis were marked in this organ.

The bone marrow revealed a marked increase in the myelogenous elements, with relative decrease in the lymphoid and erythroblastic cells. Myeloblasts were fairly numerous, while premyelocytes and myelocytes were present in great numbers. Mitotic figures were very frequent. Mature polymorpho-nuclear leucocytes were very rarely seen. The picture suggested an intensely rapid and excessive production of cells of the myeloid series, such as is seen in myelogenous leuchæmia.

From histological examination it appears that there is a mild myeloid transformation of spleen, liver, kidney and bone marrow, much as in myelogenous leuchæmia, though in mild degree. A slight myeloid change of this description is not sufficient proof of leuchæmia, for such a mild proliferation may occur in the severe anæmias and in many forms of infection.

The clinical history and the blood picture of this patient are unlike those of any leuchæmia. Apparently a coccal infection over a period of about three weeks had caused a stimulation of the leucoplastic activity of the bone marrow. As the infection progressed, the polymorpho-nuclear neutrophile leucocytes were overwhelmed and, instead of the leucopenia which often follows in somewhat similar cases from paralysis of the activity of the marrow, intense stimulation of the formative tissues resulted in the production of immature neutrophile cells in several different situations—liver, spleen and kidney, as well as in the bone marrow. Shortly before death came the final effort on the part of the formative tissues to respond to the unceasing stimulus, the result being the flooding of the circulation with immature cells, mostly of the myelocytic type, though a certain number of still earlier forms were present. It seems more reasonable to assume that this specific neutrophilic response is the result of the coccal infection rather than to imagine that a latent leuchæmia was present and that the pneumonia and empyema resulted from an intercurrent infection.

The difficulty in the diagnosis of these cases from leuchæmia is obvious and such histories strongly suggest that the leuchæmic diseases are marely exaggerated responses to some unknown toxic agents.

Similar in this respect are those cases classed together under the term "acute infectious lymphoblastosis." Sprunt and Evans[23] described six cases which were characterized by a mononuclear leucocytosis in reaction to an acute infection along with a general moderate enlargement of the lymphatic glands and the spleen. Similar cases have been described by Türk,[24] Lüdke,[25] Cabot,[26] Sanders,[27] Bloedorn and Houghton,[28] Longcope[55] and others, most of them emphasizing the resemblance of these cases to acute leuchæmia. The condition, however, is not generally recognized. The close similarity of these cases to each other in symptoms, physical signs and blood picture gives them a well-defined position as a clinical group, though they are probably due to various ætiological factors. There is usually a history of malaise for a week or more, with headache and frequently sore throat or cough from infection of the tonsils or upper respiratory passages. There is general moderate glandular enlargement and often a palpable spleen which may rapidly increase in size until it reaches nearly to the umbilicus.

A fair degree of fever is usually present, the temperature ranging from 37.2° C. to 39° C. or 39.4° C. (99° F. to 102° F. or 103° F.) for ten days or more. Generally within a fortnight the patient is out of bed. The blood picture in a few weeks returns to normal, but the glandular enlargement may be detected months afterwards. The blood picture at the height of the disease shows an increase in the cells of the large mononuclear group and the presence of many pathological lymphoid forms.

Sprunt and Evans[23] conclude that, in addition to the simple lymphocytosis often seen in children, a mononuclear leucocytosis made up largely of pathological forms, probably of lymphoid origin, may

occur in adults in response to an acute infection. When such patients are first seen in the early stages, leuchæmia cannot with certainty be excluded, but the subsequent benign course, with early disappearance of the fever and the gradual return of the blood picture to normal, makes the diagnosis clear.

Within the past eighteen months I have seen two patients whose condition belongs to this clinical group, while Dr. J. Newman Morris has kindly sent me clinical notes of two others whose blood films I have examined on several occasions. In all of these patients the suggested diagnosis of acute leuchæmia happily proved to be without foundation.

The following case history illustrates the difficulty of diagnosis:

C.M., male, aged twenty-three years, was admitted to hospital on November 23, 1921, with the diagnosis of typhoid fever. The present illness had commenced twelve days before with headache and abdominal pain, followed three days later by epistaxis. The appetite was lost and the bowels were constipated. The temperature was 38.5° C. (101.4° F.), the pulse rate 98 and the respirations 26.

The spleen was palpable four fingers' breadths below the costal margin and the cervical lymphatic glands were enlarged. Laboratory examination for evidence of enteric infection was resultless. Blood examination showed 50% of so-called "large lymphocytes" in a total count of 8,500 leucocytes per cubic millimetre.

The diagnosis of acute leuchæmia in an early stage was suggested.

On November 26, 1921 (three days later), the patient complained of a sore throat. The temperature was 39° C. and the pulse rate 96. The tonsils were large and engorged, showing a follicular exudate which in the course of a few days extended to form a pseudo-membrane. No *Bacilli diphtheriæ* were found on examination.

On December 3, 1922, the temperature, which previously had been ranging between 37.2° C. and 38.3° C. (99° F. and 101° F.), became normal.

On December 5, 1922, the throat was all right, the glands were decreasing in size, while the blood film still showed preponderance of large lymphocytic forms. There were 12,100 leucocytes per cubic millimetre three days later, when the patient was discharged.

A year afterwards the patient was in excellent health. His blood was not examined.

The importance of accurate diagnosis in these cases is forcibly illustrated by the history of a boy seen nine months ago by two consultants. Both agreed with the provisional diagnosis of acute leuchæmia and the prognosis of rapid death.

Cables detailing the clinical history were sent to leading clinics throughout the world and Dr. Mayo replied that the case was probably one of this group with a good prognosis. At present the boy is well and, apart from some persistent general glandular enlargement, shows nothing abnormal on examination.

Most of the recorded cases have occurred in young adults and have usually been associated with tonsillitis or some infection of the upper respiratory tract. The abnormal cells present in the blood, the so-called "large lymphocytes" or large mononuclear cells, are probably lymphoid in origin. They resemble the cells found in some cases of acute leuchæmia. Thus, in response to infection, affections arise with a hyperleucocytosis affecting the granular cells, with or without pathological immature types in the blood and also affections with a hyper-lymphocytosis, especially in children, while particularly in young adults pathological lymphoid forms may appear in the circulation with or without an increase in the total number of leucocytes.

All these conditions have a certain resemblance to the leuchæmias and perhaps our conception of leuchæmia requires to be broader. In this connexion a number of interesting cases reported in the literature may be mentioned. Tuohy[33] reported a case with splenomegaly and 99% of polymorpho-nuclear neutrophile cells in a total count of 65,000 leucocytes per cubic millimetre. Three days after splenectomy the white count rose to 240,000, subsiding in a month to 45,000 white blood cells per cubic millimetre. The patient died of pneumonia seventeen months later, but no further investigations could be made.

Simon's[29] case of a fractured tibia with coccal infection was associated with splenomegaly and a neutrophile myelocyte count of 15% and a mast cell count of 17.5% in a total of 50,000 leucocytes per cubic millimetre.

Giffin[30] reported the history of a patient who before operation showed splenomegaly and an eosinophilia of 73.6% in a total white count of 21,800. After splenectomy the count rapidly increased to 79% of eosinophile cells in a total count of 97,200. Nearly three years later there was 90.7% of eosinophile cells in a total count of 211,000. The long duration of the disease and the rarity of immature eosinophile cells in the blood film along with other findings suggested that the case was one of eosinophile hyper-leucocytosis rather than of leuchæmia. Stillman[31] and McDonald and Shaw[32] have reported very similar cases. The latter observers are inclined to look on these cases as leuchæmias of special type and suggest that a wider conception of leuchæmia is perhaps necessary to include these and other rare allied cases with specific affection of neutrophile, eosinophile, basophile or lymphocytic elements respectively.

In the preceding paragraphs an attempt has been made to show the gradual transition from the normal leucocytic response to various infections or intoxications through the more abnormal hyperleucocytoses with mature cells predominating and on to the cases with or without hyper-leucocytosis, but with immature cells predominating, whence it is but a step to the leuchæmias, leuchæmic, subleuchæmic and aleuchæmic. Practically the whole process can be traced by easy steps through its various stages and so we come to discuss the other side of the picture and try to follow the process through to the tumour-like infiltrations of a leuco-sarcoma or chloroma.

The Leuchæmias.

The histological picture met with in the leuchæmias is one of infiltration of the spleen, lymph glands and bone marrow with the predominant cell type seen in the blood. This may be so evident as practically to obliterate the normal architecture of these organs. Between the columns of liver cells, the dilated sinusoids are full of similar cells which show no tendency to infiltrate and destroy the liver cells actively, any destruction of the hepatic cells being due merely to a mechanical pressure atrophy.

The connective tissue of the periportal spaces is also infiltrated with these cells.

In the kidney likewise a huge infiltration may take place, the cells sometimes being accumulated in great numbers between each individual tubule, but showing no tendency to active infiltration and destruction of the parenchyma of the organ itself.

Similar infiltration has been described in practically every organ in the body. The extent of the process will vary with the acute or chronic course of the disease, while the predominant type of cell will vary both with the acuteness or otherwise of the case and with the myeloid or lymphatic response.

As Webster[35] points out this picture of the typical histology of the leuchæmic process, with its infiltrating cells not actively destructive, with its diffuse infiltration about every portal canal in the liver, about every Malpighian body in the spleen and about every kidney tubule and glomerulus, is quite unlike that of any malignant tumour.

Leuco-Sarcoma.

From this typical picture Sternberg separated a group of cases under the term leuco-sarcoma, characterized by a leuchæmic blood picture and an invasive lymphoid tumour which might arise in any situation, though occurring most commonly in the mediastinum. Such a condition usually occurs in children or young adults, the majority of patients reported in the literature being under thirty years of age.

The situation most commonly affected is the mediastinum and hence the most prominent symptoms are usually those of a mediastinal tumour, cough, dyspnœa, dysphagia, aphonia, inequality of the pupils, dilated veins over face and neck, suffusion of the face, inequality of the right and left radial pulse and so on, symptoms due to pressure on the important structures in the mediastinum. Malaise, loss of weight and enlargement of the glands are the only other common symptoms. Examination reveals enlargement of the liver, spleen and glands, with the blood picture of a lymphatic leuchæmia and, in addition, an invasive tumour mass, usually in the mediastinum, but sometimes in other situations, such as the skull or breast. Death occurs in most cases in about six months. Very rarely does the disease last for a year.

Post mortem examination shows the general glandular enlargements and the infiltration of bone marrow and other organs, as in leuchæmia, and, in addition, the invasive tumour, usually mediastinal, spreading to involve pleura and pericardium. Microscopically there is uniform infiltration of the organs and bone marrow with the same type of lymphoid cells as is found in the tumour.

L. T. Webster,[36] in a very instructive analysis of one hundred and twenty-three cases of lymphatic leuchæmia and allied conditions, reports an interesting case of leuco-sarcoma which showed three distinct clinical phases: first, a five months' history of mediastinal pressure symptoms without leuchæmia, followed while under observation by a leuchæmic blood change with definite leuchæmic symptoms, the tendency to hæmorrhage being particularly marked and, finally, a terminal stage of symptoms due to secondary anæmia. Here a localized invasive mediastinal tumour (so-called lympho-sarcoma) changed to a leuco-sarcoma.

He also details the history of a patient with chronic lymphatic leuchæmia of some three years' duration. In the last month there was a great increase in size of the inguinal glandular enlargements, which were seen at necropsy to invade the skin, peri-glandular tissue, fascia and periosteum covering the ilia, the retro-peritoneal tissues and the pancreas.

These case histories strongly suggest that all these conditions, so-called lympho-sarcoma, leuco-sarcoma and the lymphatic leuchæmias, are really different manifestations of the same disease.

Chloroma.

Chloroma appears to differ only in degree from the other leuchæmic processes, so that Sternberg included it among his cases of leuco-sarcoma.

It is usually characterized by a leuchæmic blood picture of either myeloid or lymphatic type, though aleuchæmic conditions of the blood have been observed, while, in addition, there are invasive, greenish tumours of the various bones, particularly the skull, vertebræ, sternum and ribs, as well as of the different organs. The green colour of the growths is not characteristic, as it is also seen in typical acute leuchæmia. The lymphatic type is stated to be more common.

The disease occurs chiefly in young males and is usually fatal within six months. As the tumours appear most frequently in the skull, the early symptoms are often referable to the eye, ear, nose or throat. In the lymphatic type some glandular enlargement is practically always evident, as it usually is in the myeloid type also. The bone marrow, spleen, in fact every organ in the body, may show leuchæmic deposits.

Only one case in the records of the Melbourne Hospital in the last thirteen years is a possible example of chloroma and the history and investigation of the case both before and after death is unfortunately far from complete.

The history is as follows:

S.D., a male, aged seventeen years, was admitted to the hospital as a possible example of acute infective endocarditis. The past history and family history were clear. The present illness had started three weeks previously, when quite suddenly his legs gave way under him. From that time he had become gradually paler and increasingly short of breath on any exertion. There were no symptoms referable to the urinary or gastro-intestinal tracts. There was no cough and hæmoptysis had not occurred. Frontal headaches with blurred vision had been troublesome for a fortnight, while more recently hæmorrhage from the gums had been present.

Examination revealed purpuric spots all over the body. Pallor was marked, but wasting was not noticeable. There was no palpable enlargement of spleen, liver or lymphatic glands. A systolic murmur was noted over the præcordium, but otherwise physical examination revealed nothing abnormal. The blood showed the presence of an intense anæmia, the red cells numbering 725,000 per cubic millimetre, with hæmoglobin 15%, while there was a predominance of so-called large lymphocytes in a count of 13,000 leucocytes per cubic millimetre.

Blood culture twice showed *Staphylococcus aureus* to be present (probably skin contamination), while occult blood

was present in the fæces on one occasion. Irregular fever up to 37.8° C. (100° F.) was present during the ten days the patient survived after admission to hospital.

Necropsy revealed hypostatic congestion of the bases of the lungs and flecks of hæmorrhage under the pericardium. The liver, spleen, kidney and lymphatic glands were apparently normal macroscopically, apart from the effects of the anæmia.

The bone marrow was paler in colour than normal, but no note is made as to its distribution. Arising from the posterior aspect of the sternum were three flattened, smooth, firm elevations of greenish colour with paler bands running through the greenish tissue. These masses arose from the periosteum and were adherent to the bone, though on separation the bone was quite smooth. It is unfortunate that the only microscopic specimen available is that from one of the tumours. This shows masses of lymphoid cells, with large, active nuclei filling most of the cell, evenly distributed on a reticulo-endothelial stroma which is most marked on the sides where the lymphoid cells have fallen out, leaving the large endothelioid cells with vesicular neuclei easily visible. At the periphery of the specimen the predominant cells become elongated with oval densely and uniformly stained nuclei. In other places there is evident proliferation of the fibrous stroma.

The blood vessels show no thickening of their coats. The cells contain no pigment granules or inclusions which might be the basis of the green tint observed macroscopically.

scopically. The section rather suggests that the condition was a round celled periosteal sarcoma of the sternum tending towards a spindle celled type.

The true chloromata fall into line with the other leuchæmic processes, being merely a somewhat aggressive type in certain situations.

Lympho-Sarcoma.

This term is in common use, but it is an unsatisfactory one, as the conditions about to be described have nothing to do with primary sarcoma of lymphatic glands. Kundrat[39] separated off from the pseudo-leuchæmias a small group of cases originating from a group of lymphatic glands or from adenoid tissues of mucous membranes, spreading by local invasion only through the lymphatics. These cases have no leuchæmic changes in the blood, while the systemic character of the leuchæmic process is absent, the trouble being purely local.

Closely allied to these cases are those which, in addition, present further extension to kidney, liver, spleen, glands, bone marrow and other organs. Clinically two groups of these cases are recognized, the abdominal and the mediastinal groups. The former in particular tends to occur in young individuals. Death usually results in both groups within a year of the onset of symptoms, which are mainly gastro-intestinal in the abdominal type, while in the other group the symptoms are those of a mediastinal tumour.

Examination may reveal abdominal masses or enlarged superficial or deep glands. In the abdominal cases, single or multiple tumours of the small intestine or mesenteric glands spread locally through the lymphatics to infiltrate the retro-peritoneal tissues, organs and glands.

The spleen, liver, glands, kidney and bone marrow are also frequently involved, these lesions being due to another mode of spread by the blood stream, as will be explained later.

Microscopically large lymphoid cells with active nucleus are usually found infiltrating the intestinal wall and the various organs.

Obviously a close relation exists between lympho-sarcoma, leuco-sarcoma and typical leuchæmia and this relation is emphasized when the more atypical leuchæmias, such as the aleuchæmic leuchæmias, with general infiltration of the organs, and leuchæmia with more localized glandular involvement, are considered. Microscopically the distant lymphatic glands, the parenchymatous organs and even the bone marrow are indistinguishable in these conditions. It is only in the accident of invasion, either of the tissues locally or of the blood stream, that these conditions differ. Webster[36] considers that they are different manifestations of the same disease and proposes to class them together under the term lymph-adenosis, leuchæmic and aleuchæmic. It is impossible to diagnose this condition early and definitely from the examination of a single gland, for the cases of acute infective lymphoblastosis also give rise to a similar histological picture of predominating homogeneous mass of lymphoid cells obliterating the normal architecture of the gland.

In all these conditions there occurs a lymphocytic proliferative response.

Hodgkin's Disease.

In Hodgkin's disease, on the other hand, there occurs typically a different and characteristic response of the reticulo-endothelial cells, leading to obliteration of the normal architecture of the gland, definite increase in the stroma, often going on later to marked fibrosis, reduction in the total number of cells, but especially of the normal lymphocytes, and an increase of endothelial cells, with giant cells and eosinophile cells frequently present.

Acute cases lasting four and six weeks have been reported by Hirschfeld and Isaak[37] and Bietzke[38] with the characteristic structure of Hodgkin's granuloma. As Ewing[40] states, apart from the specific structure presented by typical stages of the process and the variations which are readily derived from it by varying proportions of the component cells, the scope of this granuloma is difficult to determine. Very early lesions are often typical and the terminal stages are commonly recognizable. The locally invasive and destructive properties of the cells of Hodgkin's granuloma and of the cells of leuco-sarcoma and allied processes have suggested that these processes are malignant. Similar lesions are, however, seen in tuberculosis.

For the present it is probably better to limit the term Hodgkin's disease to the clinical and pathological entity, the main features of which are usually painless, discrete, glandular enlargements, generally starting in the cervical region, often later associated with enlargement of liver and spleen, with no leuchæmic changes in the blood, but with the specific histological picture detailed above. It is an endothelial-stroma proliferative process in contrast to the lymphocytic proliferative processes of the lymph-adenoses.

It is probably, as Galloway[34] states, a general specific disease of infective orgin with progressive infection of susceptible structures. Later, when the ætiology of these conditions is known, it will probably be found that this conception of Hodgkin's disease is too limited, but until then this restriction

of the term to those cases with the typical histological picture enables a definite diagnosis and prognosis to be given from the examination of a single gland.

Pappenheim's[10] conception of the rôle of the reticulo-endothelial system in these processes provides a good foundation on which to build ideas. As has been stated before, he regards the peri-vascular endothelial cells throughout the whole reticulo-endothelial system as the blood cell formative tissues of the body.

Leuchæmia thus becomes, not a disease of the bone marrow or lymphatic glands, but a disease of the diffuse myeloid or lymphatic tissues throughout the whole body. In leuchæmia the endothelial cells give rise to the typical cells which make their way into the blood stream in the leuchæmic stages, but which, in the aleuchæmic phases, find access to the blood stream difficult.

In lympho-sarcoma the direction of growth is away from the blood stream, infiltration occurring locally along the lymphatics. This explains Kundrat's[39] local form of lympho-sarcoma. The irritant exciting proliferation in these cases probably travels slowly by the lymph stream and is more or less localized. The general infiltration of the parenchymatous organs which occurs in some of these cases, is explained by the diffusion of the irritant widely by way of the blood, again leading to proliferation of the perivascular endothelial cells in the various organs with growth away from the blood stream. In leuco-sarcoma the direction of the growth is both locally along the lymphatics giving rise to the local invasive tumour and into the blood stream with the resultant leuchæmic blood picture.

Chloroma may be similarly explained.

These conditions are probably all manifestations of the same disease, the varying picture depending on the direction of growth of the endothelial cells in response to the stimulus and possibly on the manner in which the stimulus reaches the affected part, whether by blood or lymph stream.

Hodgkin's disease similarly falls into line as a response on the part of the reticulo-endothelial cells to a different irritant, the result being the predominance of a different cell type. The type of irritant with its affinity for a particular series of cells, its position (whether acting in blood or lymph stream) and the constitution of the patient, among other factors, will influence the pathological process and so cause the variations found in the clinical pictures of these diseases.

THE ÆTIOLOGY OF LEUCHÆMIA.

The traumatic theory of leuchæmia was one of the earliest brought forward to explain this disease. Trauma is probably a coincidence in most cases, sometimes perhaps perdisposing to leuchæmia (compare traumatic pneumonia).

Ziegler[41] suggested that leuchæmia was produced by the upset of the normal balance between the myeloid and lymphatic tissues in some way or another. However, a primary atrophy of one tissue is not found in leuchæmia, such atrophy, when it does occur, always being secondary.

Naegeli suggested that the disease was due to loss of balance in the control exercised by the ductless glands over the blood-forming organs. But there is no evidence of primary pathological lesions in the ductless glands in leuchæmia. Such derangements as occur are secondary to the leuchæmia.

Various observers consider that the leuchæmias are really malignant tumours. But the typical histological picture of leuchæmia, with its infiltrating, but not destructive cells, the diffuse infiltration about every portal canal, every Malpighian body and every kidney tubule, is entirely different from the single primary focus of a malignant tumour with its widely scattered and more or less numerous metastases.

Sternberg compromises by considering that lympho-sarcoma, leuco-sarcoma and chloroma are malignant tumours essentially different from the leuchæmias. But it has already been shown that all these conditions are probably varying manifestations of the same disease. The various infective granulomata may lead to invasion and destruction of surrounding tissues, yet they are not classed with the neoplasms.

The theory of infection as originally proposed rather favoured the idea of a specific infection in these cases, but it is quite probable that the leuchæmic process is a response to various irritants in a person predisposed to this condition.

There are several cases in the literature which strongly suggest the communication of the disease by contagion. Such cases are reported by Obrastzow,[43] Cabot[44] and Bie.[45]

Arnsperger[46] reports a series of cases suggesting that at times leuchæmia may be endemic.

Interesting reports of the family occurrence of leuchæmia are noted by Barrencheen[47] and Cameron[48] among others.

Though these reports in the literature are comparatively rare, they are somewhat suggestive of the infective origin of this condition.

Finally, attempts to transmit leuchæmia from one animal to another have been made. Only Schupfer[49] has attempted an homologous experiment with human material when he unsuccessfully injected leuchæmic blood into four patients suffering from cancer.

Heterologous grafts fail to produce leuchæmia, but homologous grafts in the fowl have given positive results. Ellerman[50] has succeeded in transmitting the disease to healthy fowls after all cellular and ordinary bacterial forms have been removed from the injected material by passage through a Berkefeld filter (No. 12). As the leucosis of fowls may be coordinated with the leuchæmias of man, the infectious nature of the disease in fowls suggests the probability of the infection theory being correct in human leuchæmia.

It has been shown in the course of this paper that there is a gradual transition from a normal blood picture through the ordinary leucocytosis due to infection and on through infective hyper-leucocytoses to the leuchæmias whose pathology is best explained on the assumption of the general diffusion of some toxic agent.

Clinically the acute leuchæmias are very similar

to the acute infectious diseases with which they are often confused.

Also in the more chronic types of the disease the irregularly raised temperature, the anæmia and the prostration suggest a more chronic, less virulent infection, which may light up into a terminal acute process.

It would seem most reasonable to assume that the leuchæmias result from the action of some toxic agent or agents widely diffused throughout the body. This toxic agent may be specific and is probably derived from a living organism, but it is quite possible that there are several such irritants which in a person predisposed to leuchæmia, may cause this disease.

TREATMENT.

Recovery from true leuchæmia is unknown. Of the agents commonly employed in the treatment, benzol, X-rays and radium, the majority of investigators favour radium. In the remissions the patients are very susceptible to intercurrent infections, hence great care should be taken to guard against such infection.

The spleen apparently has little to do with leuchæmia and splenectomy is not advisable. If it is done at all, the size of the spleen should first be reduced by radium. The only splenectomy for this condition which has occurred in the Melbourne Hospital in recent years, was followed by death from heart failure in a few hours and the dilated abdominal vessels seen *post mortem* suggested the advisability of applying a fairly tight abdominal binder after the huge organ was removed from the abdomen.

Lindstroem[51] produced a leucotoxic serum by immunizing a sheep against the leucocytes of the rabbit. Intravenous injection of this serum produced in rabbits a fall in the number of leucocytes going on to death, though in each case there was first a transient stimulation of leucocytic production with relatively small doses. This was tried on four human patients with myeloid leuchæmia with inconclusive though suggestive results. Ordway and Gorham[14] have produced an active leucolytic serum by repeatedly injecting into a rabbit white blood cells from cases of human myeloid leuchæmia, though they do not state whether it was used in the treatment of this condition.

As certain acute infections respond to non-specific protein therapy and as the leuchæmias are in all probably due to some infective agent, it was considered advisable to investigate the results of the intravenous injection of a vaccine of *Bacillus typhosus, Bacillus paratyphosus A* and *Bacillus paratyphosus B* in a case of acute myelogenous leuchæmia. This particular vaccine was chosen for two reasons, the first being that this vaccine given subcutaneously depresses the leucoplastic activity of the bone marrow with regard to the formation of granular leucocytes (see Table IV.) and so a specific as well as a non-specific effect might be obtained. The second reason was to enable an investigation of the antibody content of the blood to be made. It is frequently stated that the body in leuchæmia is unable to produce agglutinins.

Moreschi[62] in twelve cases of leuchæmia following the injection of typhoid vaccine subcutaneously was able to detect very little or no formation of agglutinins, nor was there any local or general reaction to the vaccine.

Patterson, Johnston and Williams[53] have shown that in the non-typhoid patient who is given an intravenous injection of typhoid-paratyphoid vaccine, the maximum agglutination is very high and is reached about the tenth day after the injection. The patient with acute leuchæmia had been given prophylactic injections of stock typhoid vaccine while on active service and just before he received an intravenous injection of vaccine containing *Bacilli typhosi* (one hundred million) and fifty million each of *Bacilli paratyphosi A et B*, his serum gave a positive Widal reaction with *Bacillus typhosus* in a dilution of one in two hundred, with *Bacillus paratyphosus A* in a dilution of one in forty and with *Bacillus paratyphosus B* in one in eighty. Ten days later the respective dilutions in which his serum gave a positive Widal reaction were one in 10,250 with *Bacillus typhosus*, one in 5,125 with *Bacillus paratyphosus A*, while with *Bacillus paratyphosus B* it still remained at one in eighty.

Obviously in this case of acute leuchæmia there was little, if any, failure of the power of the body to produce agglutinins.

The history of this patient is interesting from many aspects:

F.C., a male, aged twenty-eight years, was admitted to hospital on March 19, 1923, with the diagnosis of possible acute Hodgkin's disease. The family history was clear. The patient had been right through the war, from 1914 to 1918, being "gassed" on one occasion and wounded on another, while in Egypt he had nearly died from dysentery.

For some six months before admission he had been "off colour," largely as the result of overwork and worry.

The present illness began a fortnight before admission, when the gums became swollen. Shortly after this he consulted a dentist, who removed a small portion of the gum for histological investigation. The pathologist's report was that very extensive cellular accumulation was present in the sub-epithelial tissues, suggesting an inflammatory rather than a neoplastic condition.

Five days before admission the cervical glands became noticeably enlarged and the following day the enlargement of the inguinal glands was observed.

There has been no bleeding. For the past few days he has been getting weaker. Latterly diarrhœa has been troublesome, mucus, but no blood, being present in the stools.

The patient looked in good health and his colour was normal. The gums were hyperplastic, soft, hyperæmic and swollen, so that in places they extended on to the opposing surfaces of the teeth of both jaws. Food collected in the pockets between the gums and teeth and infection resulted in the formation of pus in this situation.

There was dulness and some tenderness over the *manubrium sterni*. Otherwise examination of the chest revealed nothing abnormal. The spleen was palpable, coming down on deep respiration about two fingers' breadths below the costal margin. The liver was slightly enlarged.

The cervical glands were swollen and showed some periglandular inflammation.

The inguinal glands were large, discrete and elastic.

In the next few days the axillary glands became much enlarged.

A band of inelastic skin about seven and a half centimetres (three inches) wide with considerable thickening, rather suggesting the feel of soft leather, extended transversely over the upper part of the abdomen and the lower part of the chest. A similar condition was noted on the forehead, particularly on the right side. This skin on the forehead pitted on pressure.

Numerous nodules were present in the skin of the back and shoulders.

These were said to be of very recent appearance, probably due to cellular infiltration, though they somewhat resembled the scars of *acne vulgaris*. The bleeding time was two and a half minutes. The coagulation time and the corpuscular fragility were normal. The red blood cells numbered 5,050,000 per cubic millimetre, with 90% of hæmoglobin (Sahli).

There was little abnormality of the red cells, though very rarely a nucleated red blood corpuscle was seen in the films.

There were 24,000 leucocytes per cubic millimetre. The predominant cell in the films was of the premyelocytic type. These cells were large, the diameter varying between 14 μ and 20 μ, with a slightly eccentric round or oval, finely woven, fairly deeply staining nucleus which occupied a large portion of the cell and contained several nucleoli.

The cytoplasm was foamy, fragile and fairly deeply, though not intensely, basophilic, while a beginning fine granulation was visible in the majority of the cells. Myelocytes were rarely seen, while the majority of the polymorpho-nuclear neutrophile leucocytes in the films were very mature, the average number of lobes to the nucleus being 3.75.

These comparatively few mature leucocytes were perhaps the survivors remaining from the normal production of the granular cells before the onset of the illness about a fortnight ago, while since that time the bone marrow activity had run largely to the production of the very immature cells which predominated in the blood film.

Some albumin was present in the urine.

For a fortnight after admission the patient's condition remained much the same. On April 6, 1923, he complained of dimness of vision. There was nothing abnormal seen on ophthalmoscopic examination. Shortly afterwards he became very dyspnœic, while the face and upper portion of the back were very cyanosed.

Signs of fluid were found at the bases of both lungs. Next day his condition was worse; the signs of fluid in the chest had extended and that night the patient died.

Throughout his stay in hospital the temperature had been swinging; during the first week from 36.6° C. to 37.8° C. (98° F. to 100° F.), in the next week from 37.2° C. to 39° C. (99° F. to 102° F.) and in the last week from 37.8° C. to 39.5° C. (100° F. to 103° F.).

The whole course of the illness had been barely five weeks.

Necropsy showed deep purple staining of the skin of the face, arms and back. Both pleural cavities contained a considerable amount of straw-coloured fluid. The lungs were collapsed, with some fibrinous lymph at both bases. A large, hard, persistent thymus overlapped the pericardium above, but there was no infiltration of the surrounding tissues. The bronchial glands were soft and only slightly enlarged. The mesenteric glands were large and soft, while the large glands in the meso-sigmoid were very hard. The superficial glands were definitely enlarged, though in no situation were the glandular enlargements massive. There was a definite nodule in the anterior part of the left side of the diaphragm.

The spleen weighed 595 grammes (twenty-one ounces). It was paler and more fleshy than usual, with some perisplenitis.

The liver and kidneys were larger than normal (liver weighed three kilograms or one hundred and seven ounces), but macroscopically there was little alteration in structure.

The bone marrow of the middle of the shaft of the femur was a deep maroon colour, with no trace of fatty tissue macroscopically.

Microscopically the marrow from the ribs showed that the predominant cell was identical with that in the blood—a premyelocytic type that has been described above.

There was a decided diminution in the relative amounts of lymphoid and erythroblastic tissue in the marrow.

Sections of the skin and of the various organs and glands were taken for microscopic examination. These show the typical infiltration of these organs with the cell type that predominated in blood and bone marrow.

About a fortnight before his death the patient was

TABLE V.—THE WHITE BLOOD CELL RESPONSE TO INTRAVENOUS VACCINE THERAPY.

Date.	Time of Day.	Total Count.	Predominant Immature Cell of Premyelocytic Type.		Polymorpho-nuclear Neutrophile Cell.		Polymorpho-nuclear Eosinophile Cell.		Polymorpho-nuclear Basophile Cell.		Lymphocytes.		Nucleated Red Blood Corpuscles.	
			Per-centage.	Total Number Per Cubic Millimetre.	Per-centage.	Total Number Per Cubic Millimetre.	Per-centage.	Total Number Per Cubic Millimetre.	Per-centage.	Total Number Per Cubic Millimetre.	Per-centage.	Total Number Per Cubic Millimetre.	Per-centage.	Total Number Per Cubic Millimetre.
March 24, 1923	10 a.m.	31,000	90.7	28,125	4.1	1,275	0.5	155	—	—	4.6	1,425	—	—
	10.40 a.m.	32,000	90.6	29,000	4.4	1,400	0.2	65	—	—	4.8	1,540	—	—
	11.10 a.m.	11,000	80.6	8,870	2.2	240	1.0	110	0.2	20	16.0	1,760	0.4	44
	2.10 p.m.	8,000	66.8	5,350	19.6	1,565	1.2	100	—	—	12.4	1,000	—	—
	7.10 p.m.	30,000	89.6	26,880	8.6	2,580	—	—	—	—	1.8	540	—	—
March 25, 1923	9.30 a.m.	40,000	90.8	36,320	5.0	2,000	0.9	360	—	—	3.3	1,320	0.4	160
March 26, 1923	9.30 a.m.	57,000	93.5	53,300	3.2	1,825	0.5	285	—	—	2.8	1,600	—	—
March 27, 1923	9.30 a.m.	52,000	90.9	47,250	3.3	1,720	0.9	460	—	—	4.9	2,550	0.1	50
March 29, 1923	9.30 a.m.	44,000	87.9	38,675	3.6	1,585	0.4	175	0.1	45	8.0	3,520	—	—
March 31, 1923	12.30 a.m.	63,400	86.5	54,840	4.2	2,660	0.6	380	0.2	125	8.7	5,515	0.2	125
April 3, 1923..	9.30 a.m.	47,000	93.2	43,800	2.6	1,225	0.1	50	—	—	4.1	1,925	—	—

March 24, 1923: Vaccine given at 10.20 a.m.; rigor 11 a.m. to 11.30 a.m.

given an intravenous injection of a vaccine of one hundred million *Bacillus typhosus* and fifty millions each of *Bacilli paratyphosi A et B*. A preliminary count was done at 10 a.m., twenty minutes before the vaccine was given and another count was done twenty minutes after the injection, but before the patient commenced to shiver. These two counts were practically identical. Ten minutes after the commencement of the rigor, the third count was done and this showed distinct changes in the cell formula. Details of these counts are given in Table V. and the more important observations are shown in the graph (see Figure I.).

The accompanying graph illustrates more forcibly the variations in the blood formula in response to this condition. To avoid confusion the total count is not illustrated, as it follows very closely the graph of the type cell. Similarly the eosinophile and basophile variations are not shown, as the margin of error is very great with such small numbers.

It is seen that early in the rigor, within an hour of the injection of the vaccine, there is a marked diminution in the total number of polymorpho-nuclear neutrophile leucocytes and in the type cell, while as yet the lymphocytes have not diminished. Three hours later the neutrophile leucocytes have increased in number, while the type cells have reached their lowest point and the lymphocytes are decreasing. Five hours later the type cells have increased definitely, while the lymphocytes are very few. Speaking generally, it is seen that the polymorpho-nuclear leucocytes show the most rapid response to the injection of the vaccine and they are fairly quickly followed by the immature cell type, while there is a definite delayed response on the part of the lymphocytes before they, too, follow a curve somewhat similar to the other cells. Dr. Burnet kindly carried out the majority of these observations for me and he suggested that by plotting the graph of the response of any particular immature cell to an intravenous injection of a vaccine, it may be possible to determine whether it belongs to the myeloid or lymphatic series. Certainly it is often impossible on morphological characters alone to decide to which class an immature cell belongs and by some such functional test we may hope to further our knowledge of the immature leucocytes.

It is usually stated that the injection of such a vaccine intravenously in a person with a normal blood picture leads to a rapid leucopenia, followed in a few hours by a leucocytosis, the whole alteration in the blood picture being due to variation in the numbers of the polymorpho-nuclear leucocytes, the absolute numbers of the lymphocytes remaining constant. As the response in the leuchæmic patient showed that there was a definite, though delayed, reaction on the part of the lymphocytes, it was considered advisable to investigate this matter. Dr. Foreman kindly placed several of his unpublished charts at my disposal. These all show definitely that in patients with rheumatoid arthritis who receive intravenous *Bacillus coli* vaccine, though the most marked response is by the polymorpho-nuclear leucocytes, there is yet a definite, though delayed, reaction also on the part of the lymphocytes. The minimum polymorpho-nuclear leucocyte count is invariably found less than two hours after the administration of the vaccine, while the minimum lymphocyte count usually occurs between three and five hours after the injection. The lymphocyte curve is in general similar to that of the polymorpho-nuclear leucocytes, but there is a definite delayed response on the part of the lymphocytes. The reason for this is unknown, but the same

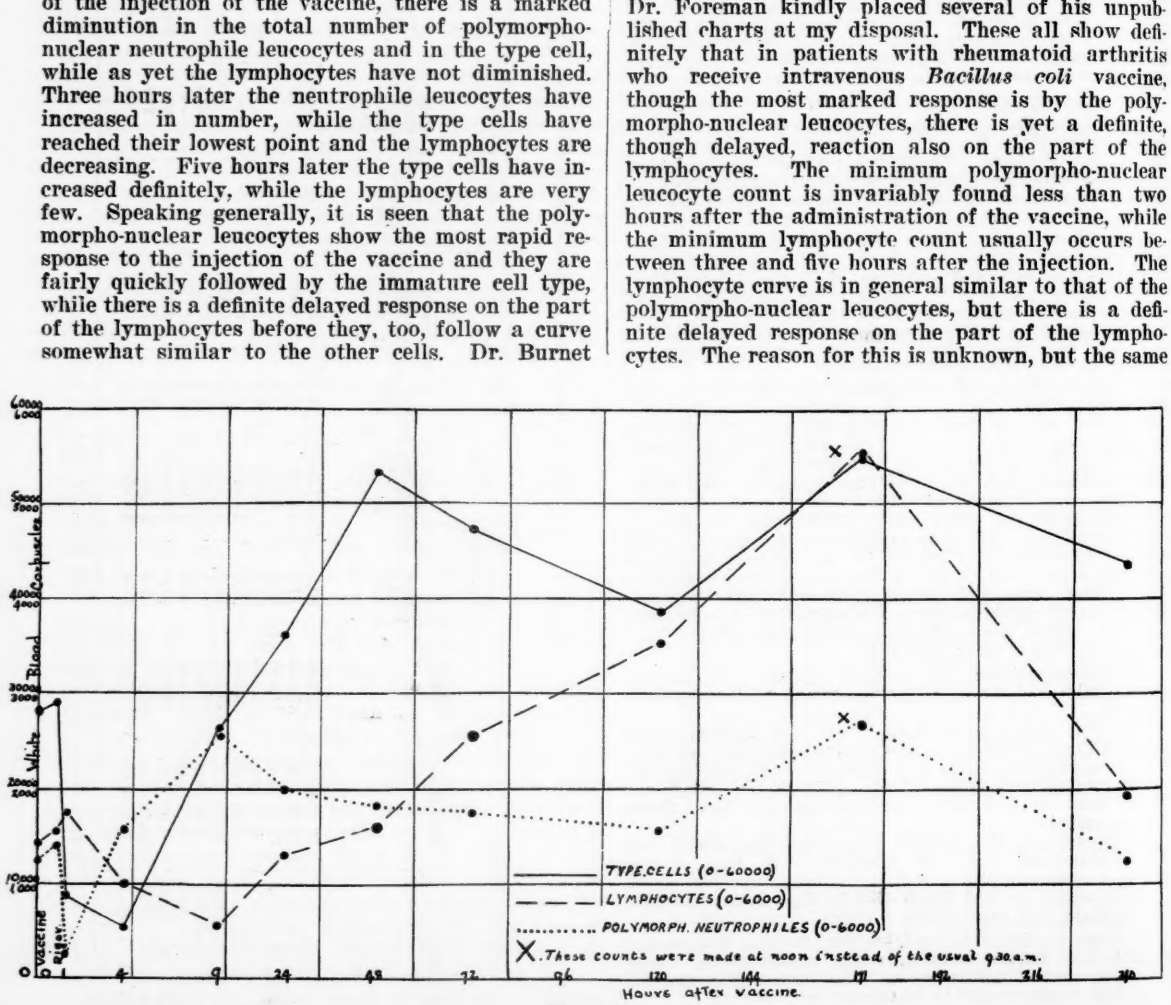


FIGURE I.

rapid response of the polymorpho-nuclear leucocytes with a more delayed reaction of the lymphocytes is seen in many inflammatory conditions.

Though, as was expected, no obvious benefit followed the single intravenous administration of the vaccine, yet the response of the various cell types was very interesting. As opportunity arises further investigations will be conducted along these lines in the various leuchæmic conditions, for it is possible that we have here a functional test which will enable us to distinguish between the various immature leucocytes, as well as give us further light on the part played in the body by the more mature cells.

CONCLUSIONS.

1. McJunkin and Charlton's[1] special stain for endothelial cells is very useful in distinguishing between the large lymphocytes and the large mononuclear cells of the blood.

2. The average normal total and differential leucocyte counts are unimportant. The limits of variation of the normal leucocyte counts are most important and these counts vary over a much wider range than is generally acknowledged.

3. The tendency to attribute some diagnostic significance to a moderately high proportion of lymphocytes in the blood in the absence of other suspicious evidence is to be deprecated.

4. In the diagnosis of acute leuchæmia care should be exercised to exclude acute infective lymphoblastosis, as the prognosis in the two conditions is quite different.

5. Lympho-sarcoma, leuco-sarcoma and lymphatic leuchæmia are probably merely different manifestations of the same disease and are better grouped under the term lymph-adenosis, leuchæmic and aleuchæmic.

6. The term Hodgkin's disease should be limited to those cases which show the typical histological changes which enable a definite diagnosis and prognosis to be made. It is probably ætiologically entirely distinct from lymph-adenosis.

7. Pappenheim's conception of the rôle of the reticulo-endothelial system enables these different conditions to be appropriately considered as variations of a single pathological process.

8. These allied conditions are probably the result of the action of toxic agents widely diffused throughout the body. Such toxic agents are probably derived from living organisms.

9. The investigation of the leucocytic response in leuchæmia following the intravenous injection of foreign protein may lead to further information with regard to the differentiation of the immature white blood corpuscles and of the functions of the leucocytes.

10. The loss of power of production of antibody is certainly not invariable in leuchæmia.

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Reviews.

DISEASES OF THE HEART.

A SMALL book on "Diseases of the Heart," by Dr. I. Harris,[1] gives us little insight into the understanding of present-day conceptions of cardiac disease. The book is loosely written and consequently it is at times difficult to grasp the author's meaning. "The course of heart failure depends on whether conditions are favourable for effective compensation or whether the condition of the heart muscle is such as not to permit of compensation." In the former case compensation "developes slowly and *pari passu* with the slow and gradual development of the lesion." In the latter case "heart failure is due to the fact that the heart muscle is not strong enough to stand an abnormal strain." These sentences, though taken out of their context, do not present the subject in a correct way, even if they convey any meaning.

The question of prognosis of chronic valvular disease is discussed according as to whether compensation is being maintained or decompensation has set in. In the former case, according to the author, the prognosis depends on the degree of the valvular lesion. In the latter case the deciding factor is the reaction of the heart to digitalis. If digitalis is ineffective, the prognosis is grave. This last statement may, of course, be correct, but if digitalis is effective in the treatment of so-called decompensation, it is effective because the rhythm of the heart is one of auricular fibrillation. That aspect is not stated.

In the discussion on the Adams-Stokes syndrome we are told that it is highly improbable that the condition is due to block of the auriculo-ventricular bundle. Most authorities would not accept that view.

There is much verbiage in the book which conveys little information. We cannot recommend it.

[1] "Diseases of the Heart: A Handbook for Students and Practitioners," by I. Harris, M.D., L.R.C.P. (Ed.); 1922. London: Baillière, Tindall & Cox; Demy 8vo., pp. xii. + 196, with fifty figures in the text. Price: 10s. 6d. net.

SOCIAL REVOLUTIONS.

PROFESSOR FRANCIS ANDERSON, Emeritus Professor of Philosophy of the University of Sydney, in a lecture entitled "Liberty, Equality and Fraternity," discusses Buddhism, Christianity, the French Revolution, the Great War and present social discontent in their relationship to the meaning of the famous motto adopted by the French people in 1793.[1] The lecturer cites Buddhism, Christianity, the French Revolution and the Great War as the four great revolutions in history. In all of them "the ideal has been one of liberty, equality and fraternity, but not the same ideal." Six centures before Christ, Siddhatha Gautama introduced Buddhism, a moral revolution without a deity. Christianity was a revolution of personal life and the French Revolution a political revolution. Modern democracy prefers equality to liberty and the rights of labour to the rights of man. To carry out the precepts of liberty, equality and fraternity in present-day society, we cannot do better than follow the advice contained in the last paragraph of the lecture: "Liberty may be won if we are willing to surrender some of our own anti-social liberties. Equality may be won if we think less of our own individual rights and more of our common duties. Fraternity may be won if we aim at that justice which is inspired by love."

This little publication, which is the forerunner of a series to be issued by the Australasian Association of Psychology and Philosophy, is well worth the time spent in studying it.

[1] "Liberty, Equality and Fraternity," by Francis Anderson, M.A., Emeritus Professor of Philosophy, the University of Sydney; Monograph Series, No. 1; 1922. Sydney: The Australasian Association of Psychology and Philosophy; Demy 8vo., paper cover pp. 24. Price: 1s..

PRACTICAL DERMATOLOGY.

"DISEASES OF THE SKIN," by Dr. Robert W. MacKenna, is an up-to-date treatise, well suited to the busy practitioner who needs a book with short, concise and yet adequate descriptions of the essential features of the various skin lesions.[2] Such a book will enable him to come to a conclusion in regard to the differential diagnosis within a short time, when he would otherwise experience some difficulty. The methods of treatment are well laid out and are not too many to follow. The directions are plain and dogmatic, which is what the busy practitioner likes. The student will find this work short and concise; the various diseases are well arranged and well classed under the several captions. This classification appears to us to be an advance on that adopted in the majority of the books on dermatology recently published. The print is clear and bold and there are one hundred and sixty-six original illustrations in the text and many valuable formulæ.

The recent advances in dermatology are described and the author gives consideration to the possible part played in the ætiology of certain skin affections by anaphylactic shock and sensitization by foreign proteins. The book can be recommended.

[2] "Diseases of the Skin," by Robert W. MacKenna, M.A., M.D., B.Ch. (Edin.); 1923. London: Baillière, Tindall & Cox; Royal 8vo., pp. x. + 460, with 166 figures in the text and many formulæ. Price: 21s. net.

The Medical Journal of Australia

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The Need for Combined Action.

BUT a few years ago the vast majority of medical practitioners derived their whole incomes from their earnings as private practitioners. In Australia there was no standing Army Medical Service with whole-time medical officers as was the case with the Royal Army Medical Corps and with the Indian Medical Service. The Navy absorbed a few medical officers and the public health services found occupation for a handful of others. All told the number of medical practitioners earning a salary in the public services in those days was so small a proportion of the total number of doctors that a standardization of the conditions of service on the basis of collective bargaining was out of the question. Modern development has brought into existence many new public and quasi-public activities in which medical practitioners are employed on salary. The public health services have been extended, the departments of public instruction have found the need for an ever increasing number of medical inspectors of school children, the Repatriation Department and the new Air Forces have tasks for medical men and women, the lunacy services have become larger and more effectively staffed, the Postal Department, the railways and tramways and factories are creating whole-time appointments for doctors and many of the public utilities, both official and charitable, find the need for the salaried services of doctors. To some this trend of affairs suggests a drift toward the nationalization of the medical profession. In reality it indicates that the application of preventive measures is becoming more and more essential and the enlistment of medical practitioners in community service is forcing itself on the profession. The movement has but started. Fresh additions to the already relatively large army of salaried medical practitioners are of daily occurrence. It is improbable that the majority will be induced to relinquish the orthodox professional plan of payment for work actually done. As long as people are attacked by disease and need medical attention from a chosen doctor, so long will the medical profession resist the intervention of a third party between the doctor and his patient. But in the larger and more important scheme of community medicine, the combating of disease and the endeavour to eradicate the causes of suffering and premature death, a third party is unavoidable. Just as the medical profession offers its services without resistance and with enthusiastic eagerness for the defence of Empire, so many medical practitioners are willing and ready to help in the national task of protecting the public health. The recognition of this important invasion of the medical profession into these public and semi-public activities necessitates a standardization of the conditions under which this work in its many forms should be conducted. The only organization of the medical profession, the British Medical Association, has hitherto refrained from intervening between individual practitioners and their patients. In regard to salaried employment a demand has been made in a few instances to fix a minimum rate of remuneration for what may be termed industrial work. The best example of this is that of insurance examination. In recent years the Federal Committee of the British Medical Association in Australia has determined the fees to be paid for insurance examinations, as a result of a generally expressed wish on the part of members. Much attention has been paid to the conditions of employment of medical practitioners as medical officers to friendly society lodges. Here again the demand of the mass of the members for the introduction of uniform conditions led to the introduction in every State of Australia of model or common forms of agreement, an example of collective bargaining which has proved of benefit to all concerned. In Great Britain the British Medical Association has special committees for Naval and Military medical officers and for medical officers in the public health services. These committees consider the conditions of service, the rates of remuneration and the status of the medical officers engaged in the services. In Australia no such committees have yet been appointed because the number of medical practitioners engaged in these services has been too small to warrant the

appointment of special bodies. Time and circumstance have changed and the demand is appearing for some organization which would undertake a watching brief on behalf of the increasing army of salaried public medical officers. At the present time this demand may be but a murmur. It has been heard in the lunacy service in one or two States and also from the part-time medical officers of health. It will become louder and more insistent as each of the separate services becomes numerically stronger. In the meantime the Branches of the British Medical Association may find it profitable to consider what machinery will eventually become necessary to protect the interests of medical practitioners engaged in the public service or in quasi-public undertakings. It is obvious that if these services are to produce the best results, if the highest degree of efficiency is to be obtained from them, the conditions of service must be attractive and the remuneration must not be less than the earnings of the average general practitioner. Otherwise the best men and women will not offer their services. There is one difficulty that will have to be overcome. Some of the services are under the control of the Federal Government and the conditions obtaining are uniform throughout Australia. Others are State services and the conditions vary according to the State. Others again are governed by conditions which are adapted according to the situation of the activities and vary even within a State. In these circumstances the same expedient that was adopted in regard to life insurance examination work, could be applied. If this expedient were followed, the first step would be the appointment by each Branch Council of a special committee with representatives from the chief services to consider the conditions of employment of salaried medical officers in the public services. The services of the Federal Committee might be requisitioned in order that the policies of the individual Branches might be coordinated and uniform conditions introduced throughout the Commonwealth. Later it might be found to be advisable to extend the reference of these committees to include the conditions of employment of medical practitioners in private salaried positions. If such committees were appointed, they would find plenty of work to do at the present time.

Current Comment.

THE TREATMENT OF BURNS IN CHILDREN.

DEATH from burns may be due either to shock which is frequently very profound, or else to what is apparently a condition of toxæmia. In either case the prognosis may be extremely grave. Confronted by these complications the practitioner is helpless to a degree. Treatment of a profound condition of shock is often hopeless. In regard to the toxæmic state the same statement usually holds good if the burns have been extensive. After the burning shock may be slight or severe and toxæmia developes after about twenty-four hours. In children especially the developments gradually become more pronounced, fever becomes extreme, vomiting sets in and convulsions occur. Pfeiffer held that death resulted from an auto-intoxication due to the destruction of protein tissue at the site of the burn and the consequent absorption of toxins. McKee showed that the urine of patients who had suffered from severe burns, was definitely hæmolytic. He found a similar condition in the urine of patients suffering from septicæmia and severe forms of shock. Leon Jona conducted experiments in regard to the effect of burns on tissues of the body. These were published in the pages of this journal in 1917 and 1918. Jona found that muscle which had been heated to 200° C. produced a small rise in temperature if injected into an animal in small quantities. If large doses were injected, a fall in temperature was noted and general symptoms were produced. These were clinical results of injection similar in every way to those produced respectively by the injection of small and large doses of bacterial emulsions or extracts. If the muscle was heated to 150° C., a small degree of reaction occurred and pyrexia was occasionally present. Similar reactions to those obtained by muscle heated to 200° C. were obtained by scorching the muscle in the flame of a Bunsen burner for a few minutes. It is interesting, moreover, to note that Jona found that the aqueous extracts of burned tissue produced a definite inhibitory effect on the action of secretin in inducing secretion of pancreatic juice in a dog. Jona held that this inhibitory action was a potent factor in the production of duodenal ulcer in patients suffering from burns. The products of the burnt tissues would, he contended, be absorbed for some time. This would inhibit the secretion of the pancreatic juice and allow the hydrochloric acid of the gastric juice to have free play on the mucosa of the duodenum. Kotzareff investigated this question and published the results of his work in 1922. He held that animals succumbed to burns unless they could manufacture antibodies or have them supplied from without promptly enough to annul the toxic action. Serum from a guinea pig that had been burned, when injected into another guinea pig, protected it from an experimentally produced burn, even when more than half the body was involved and the burn was one of the third degree. He reported fourteen instances similar to this and in addition described the recovery of two boys, aged eight and five and a

half years, after the intramuscular injection of five and eight cubic centimetres respectively of serum obtained from other children convalescing from burns. He recommended the systematic production and use of an anti-burn serum.

Dr. Bruce Robertson and Dr. Gladys Boyd have described another method of treatment which in their hands has proved satisfactory.[1] They state that the simplest method of overcoming the toxin is to remove it. To achieve this object they have devised the operation of exsanguination-transfusion. A larger quantity of blood is withdrawn from the longitudinal sinus or femoral vein than could be withdrawn by venesection and this is replaced by fresh adult blood. Withdrawal and transfusion are carried on simultaneously. The amount of blood withdrawn by these two observers varied from two hundred cubic centimetres in an infant up to five hundred cubic centimetres in a child of three years of age. Ten children suffering from toxæmic convulsions after burns were treated. Two were treated by simple transfusion and eight by exsanguination-transfusion. Three of the latter died from burn toxæmia and in the remainder the toxæmia was relieved. They state that they have not seen a child recover with any other form of treatment after the onset of convulsions. Drs. Robertson and Boyd report the results of some experiments on the nature of the toxin in burns. They have given no details, but have promised the full publication of these at a later date. They have found that there is a substance produced in burns, that this substance circulates in the blood, that it is either in or closely adsorbed to the red blood corpuscles and that it produces the characteristic symptoms of toxic shock. This toxin consists of primary and secondary proteoses and is made up of two portions, necrotoxic and neurotoxic. The former is not destroyed by heat and is diffusible; the latter is thermolobile and colloidal in nature.

INDUSTRIAL INSPECTION IN RUSSIA.

THE reports which come from Russia, are conflicting and in most instances coloured by the political views of the person or persons making the report. For this reason statements from reliable sources are valuable. Such, for instance, was the report of Dr. René Sand on the famine conditions in Russia to which reference was made in the pages of this journal twelve months ago. There has recently come to hand a copy of the *International Labour Review* for January, 1923. This publication is one of those issued by the League of Nations and statements made by the various contributors to its pages may be regarded as authoritative. In this number there appears an extremely interesting article on the present system of industrial inspection as carried out under the Soviet Government.

Immediately after the revolution in October, 1917, there followed a period of chaos and confusion in industry as in all other activities in the country. The Soviet Government, however, gradually evolved a general scheme of industrial supervision and inspection which was embodied in a decree issued in May, 1918, and subsequently incorporated in *The Labour Code* of 1918. The underlying principle was that the workers should elect from amongst their own numbers inspectors who would be responsible for the conditions of labour. A labour inspector is defined in *The Labour Code* as one who is himself a worker and therefore in touch with working conditions.

In addition to these elected inspectors it was found necessary at an early stage to appoint inspectors who had the technical knowledge necessary for the position. These technical inspectors were appointed as a result of examination and about 37% of their number had been employed in a similar capacity under the old Czarist régime. Under the Czarist Government there had been one inspector to 20,000 or 25,000 workers. It was decided to increase the number so that there would be one inspector to 7,000 or 8,000. The number of elected inspectors at the end of 1921 was 1,457 and technical inspectors at the end of 1920 numbered 129. The elected inspector is the person who makes decisions on all questions of principle. The powers of the elected inspectors are comprehensive. An inspector takes his instructions from the local labour section and from the local inter-trade union organization. Whenever possible he is accompanied by a member of the works council or of the local trade union. In important enterprises he is also accompanied by a technical inspector. He must inspect the card records of the employees, investigate the conditions of the women and children employed in the industry, inquire into the question of overtime and investigate the accident records. He must keep himself well informed on all subjects that affect the employees, both from the point of view of their work and of their welfare. He must see that his recommendations are carried out and, when this has not been done, he is required to institute a prosecution and state his case in court. One of the most important of the activities of the inspector is that of consultation. On fixed days and at fixed hours any employee may consult the inspector. These consultations are generally concerned with the granting of exemption from compulsory labour or overtime or with the employment of young workers. Not only does he give advice, but he is often called upon to make decisions on disputed points. Some idea of the activities connected with this service may be gathered from the fact that in the month of August, 1921, the number of prosecutions instituted numbered twenty-four among every hundred inspectors. The most severe punishment, that of closing an establishment, was only enforced on ten occasions during the whole of 1921. In regard to the number of consultations, there were on an average 67.7 consultations per 10,000 trade union workers during the month of August, 1921.

As a system the whole arrangements are very far-reaching, but the writer of the article under discussion states that an estimation of the actual work done is impossible. The statistics quoted are very incomplete. For example, only 10% of all the accidents are reported. The conclusion is reached that the Russion inspection is so far only in partial working order.

[1] *American Journal of Diseases of Children*, February, 1923.

Abstracts from Current Medical Literature.

GYNÆCOLOGY AND OBSTETRICS.

The Endocrine Functions of the Female Reproductive Organs.

S. VINCENT (*The Lancet*, February 11, 1922) has reviewed the present opinions regarding the functions and influence of the glands of internal secretion in the female. From the evidence of ovarian castration it seems certain that the ovary has a pronounced influence in helping to develope and to maintain the female secondary sexual characters. The *corpus luteum* appears to have the function of preventing ovulation. It also has an influence in the very early days of pregnancy in preparing the mucosa of the uterus for the embedding of the ovum by stimulating it to hypertrophy. The adrenal cortex appears to have certain important functions in connexion with the development and growth of the sex organs. Tumours of the adrenal cortex are frequently associated with sex abnormalities. When cortical tumours occur in the female there is development of the male secondary characters and hypoplasia of the internal generative organs. The adrenal cortex is enlarged during breeding and pregnancy. The thyreoid is relatively larger in women than in men, especially during puberty, menstruation and pregnancy. Sexual intercourse increases the size and activity of the gland. It is stated that the ovaries exercise an inhibitory action on the thyreoid; in fact, the latter becomes hyperactive after castration and there is an increase of the colloid substance. This is the cause, it is said, of the large number of cases of exophthalmic goître occurring in women after the menopause. The pineal gland is alleged to have an influence on sexual precocity. The pituitary has an influence on many of the metabolic functions necessary for the establishment of puberty. Removal of the thymus performed before puberty causes a rapid development of the genital gland. The whole subject is complicated by the influence of the various organs of internal secretion upon each other. The psychological characters of women are, of course, partly accidental and dependent on social conditions, but of those which are more fundamental, some depend on the influence of the ovary and others on general metabolic processes which are largely conditioned by the general reactions of the glands of internal secretion.

Acute Appendicitis and Acute Right Salpingitis.

MAURICE MARCUS (*The Lancet*, October 14, 1922) points out that in appendicitis the pain is usually first felt in the region of the umbilicus and only later in the right iliac fossa. In acute right salpingitis, however, pain is felt almost invariably and from the first on the right side. In addition the pain is usually referred down the right thigh anteriorly, sometimes as far as the knee. Other lesions of the Fallopian tube, such as ruptured pyosalpinx, ruptured ectopic gestation or ruptured ovarian cyst will cause pain with a similar distribution. A retrocaecal appendix will cause pain from the first in the right iliac fossa. The distribution of the pain in the two conditions is explained by the fact that the Fallopian tube is developed as a lateral organ and is represented in the spinal cord of the eleventh and twelfth dorsal and first lumbar segments. The appendix is medial in origin and is represented by the tenth and eleventh thoracic segments.

The Calcium and Inorganic Phosphorus Content of the Maternal Blood during Pregnancy and Lactation.

O. L. V. DE WESSELOW (*The Lancet*, July 19, 1922), in a report to the Medical Research Council, gives the results of an investigation made by him into the calcium and inorganic phosphorus content of maternal blood in pregnancy and lactation. It has been shown that there is a great demand for these elements in pregnancy and during lactation. The fœtus at birth contains 20.4 grammes of calcium, while the daily intake on an ordinary diet is only 0.74 grammes *per diem*. The writer found that there appears to be a tendency to a fall in the inorganic phosphorus, calcium and total solid content of the serum during the later months of pregnancy. During lactation the calcium and total solids are restored to a normal figure and the phosphates rise to a figure definitely above that of the non-lactating female. But, although the calcium content is lowered, it is kept within physiological limits and the demand for calcium for the fœtus is met not by depleting the maternal blood but by drawing on the calcium reserves in the maternal osseous system. After delivery the calcium value returns rapidly to a normal figure. The importance of an adequate supply of inorganic phosphorus to the active mammary gland is obvious when the relatively high phosphate content of milk and the importance of phosphates to the growing infant are considered. The inorganic phosphates of the plasma are more important than the lipoid phosphates and in the cow it was found that a diminution in the rations was accompanied by a fall of inorganic phosphorus in the plasma but no alteration in the lipoid phosphates. Lastly, the estimations of the total solids of the serum strongly suggest a progressive dilution of the blood during pregnancy, the percentage of water increasing with the length of gestation.

Cysts of the Labia Minora.

J. DUVERGEY AND J. FICHEZ (*The Lancet*, June 10, 1922), in recording an illustrative instance of a cyst in the *labia minora* in a woman aged forty, state that such cysts are comparatively rare. Only thirty were recorded in the literature examined by them. The cysts usually develope on the outer surfaces and face margins of the labia and as a rule are pedunculated. They project from the vulva and do not give rise to serious symptoms. With the exception of two instances the cysts in all those recorded were single and varied in size from a pea to an orange. The writers divide cysts of the *labia minora* into two groups, the first and most numerous being sebaceous cysts and the second being mucous cysts. Sebaceous cysts are usually situated on the outer surface of the *labia minora*, where sebaceous glands are extremely numerous. On the outer surfaces of the *labia minora*, according to Martin and Léger, they number 130 to 140 to the square centimetre, while on the inner surface the number is 28 to 30. Up to puberty the sebaceous glands remain inactive. They reach their greatest development during pregnancy. Mucous cysts have been variously regarded as of lymphatic origin, as derived from mucous glands (the existence of which in this region is doubtful) or from aberrant Bartholinian glands. The writers consider that the last is the most probable explanation. The prognosis is always favourable. Though the cyst may suppurate and give rise to a fistula, malignant degeneration has never been recorded. Treatment consists in local extirpation under an anæsthetic followed by a plastic operation on the labium. The wound usually heals within a fortnight and recurrence is unknown.

The Relation of the Thyreoid Gland to the Female Pelvic Organs.

C. M. WILSON AND A. W. BOURNE (*The Lancet*, May 27, 1922) carried out a research to define more clearly the relation between the thyreoid gland and the female pelvic organs. They used as a control an estimation of the basal metabolic rate and compared the normal rate with that found in pregnancy and the puerperium and in functional menorrhagia. A series of patients suffering from the last named condition were treated by X-rays applied to the thyreoid gland. They concluded that the basal metabolic rate is in the majority of pregnant women, but not in all, raised above that normally found in non-pregnant women. The basal metabolic rate of different pregnant women at corresponding periods of gestation varies considerably, but it was not found possible to trace any relation between these variations in the rate and the clinical condition of the mother. It remains to be determined if there is any correspondence between the fluctuations in the rate of the same patient at different times and her clinical state on the one hand or that of the child on the other. In some patients, probably the majority, the rise in the basal metabolic rate disappears after delivery, but in a certain number of instances the high rate of pregnancy does not subside after the puerperium, but abnormally persists. The suggestion is put forward that in some of the latter patients the excessive thyreoid secretion gives rise to a menorrhagia without pelvic signs. Additional evidence that a high basal

metabolic rate is associated with certain forms of menorrhagia is furnished by a group to which the label functional menorrhagia is attached and in which no pelvic abnormality is demonstrable. The condition of patients comprising this group are resistant to all ordinary medicinal and operative measures, but respond readily when the thyreoid gland is exposed to X-rays. The disappearance of pelvic symptoms is coincident with a fall to normal of the basal metabolic rate.

NEUROLOGY.

Toxic Polyneuritis.

WILFRED HARRIS, (*Brain*, Parts III. and V., 1922) classifies multiple neuritis on an ætiological basis into four groups: (i.) Those dependent on the absorption of poisons introduced into the body. (ii.) Those due to autotoxæmia or to poisons developed primarily within the body. (iii.) Those due to infections of an organismal nature. (iv.) Those occurring in cachectic states. The author in this paper deals only with lesser known types. Silver is a rare and doubtful cause of polyneuritis, carbon bisulphide and monoxide are also uncommon causes. Acute rheumatism is rarely if ever followed by polyneuritis, yet local perineuritis and fibrositis, as seen in brachial neuritis and sciatica, are common sequels of cold and exposure, though other causes such as dental or intestinal sepsis may contribute. "Chloretone" may produce a flaccid paralysis akin to polyneuritis. Local asymmetrical neuritis is a feature of typhoid and paratyphoid infections. Asymmetrical neuritis, as well as the more common polyneuritis, may also be seen in chronic alcoholism and diabetes. The polyneuritic psychosis of Korsakow may arise in patients with polyneuritis not due to alcohol. Septicæmia is a not uncommon cause of multiple neuritis, differing little from alcoholic neuritis. Acute febrile polyneuritis was frequently observed during the late war. Syphilis as a cause of polyneuritis occasionally acts as an acute infective toxæmia, as also do tuberculosis and malignant disease. Polyneuritis may be due to autotoxæmia, beri-beri, the puerperium, diphtheria and hæmatoporphyrinuria.

A Flexion Reflex of the Toes.

D. SCHRIJVER (*Revue Neurologique*, December, 1922) describes a reflex which he has observed in patients suffering from *dementia præcox*, particularly those showing catatonia. The reflex consists of flexion of the toes on percussing the anterior surface of the leg, between knee and ankle. Patients with hemiplegia and lesion of the pyramidal tract do not show the reflex, nor is it associated with any sign of organic disease of the nervous system. Since the latent period between excitation and the occurrence of movement is brief, the author is of the opinion that the reflex cannot have a cerebral localization.

The Endocrine Glands and Epilepsy.

L. MARCHAND (*Revue Neurologique*, December, 1922) has undertaken an exhaustive review of the literature and has studied the relationship of the endocrine glands to epilepsy. In spite of the numerous published reports on the possible connexion between functional disturbances of the endocrine glands and epilepsy, the author is of the opinion that the connexion is not proven. Numerous instances which at first sight appear to be conclusive, will not bear critical examination. There is but a limited number of observations in which it can be admitted that the endocrine disorder has caused the epilepsy. There are of course among epileptics some whose condition is more or less Basedowian or Addisonian in type. Others are the subject of hypothyreoidism or hypopituitarism, but such disturbance is not more common among epileptics than among other individuals.

Defence Reflexes.

J. BABINSKI (*Revue Neurologique*, August, 1922) in a paper on the defence reflexes opens by indicating that diverse names have been needlessly given to one and the same phenomenon, names such as antagonistic reflex of Schäfer, the leg phenomenon of Oppenheim, reflexts of spinal automatism of Marie, the mass reflex of Head and Riddoch. This phenomenon is the motor reaction which follows certain sensory stimuli. Thus, scratching the sole of the foot with a pin, or pinching the skin of the foot or lower leg induces triple flexion, namely, at the ankle, knee and thigh joints. Not only are there other means of exciting this reflex but the reflexogenous zone and the amplitude of the resulting movements respectively vary in extent and degree. First, concerning the connexion between the defence reflexes and the well-known toe phenomenon, the author holds that this is not unbreakable; the two do not fuse completely. Secondly, he says that all defence reflexes are certainly not pathological. Chief of all is the fact that in the normal subject the muscular contraction is rapid and brief, in the diseased, slow and sustained. Attention is next drawn to an isolated sign. If flexion of the foot alone be obtained by excitation of any part other than the sole of the foot, thus by pinching the dorsum of the foot or the lower leg, then a morbid condition can be affirmed. This, the author calls the sign of the flexion reflex of the foot and he considers that it is closely related to the toe phenomenon; both point to interference with the pyramidal tract. He goes on to show that the condition of the defence reflexes may aid in the localization of a spinal lesion and be a guide to its intensity, thus, very active defence reflexes suggest relative integrity of pyramidal tracts. Again in the first phase of spinal compression, the toe extension sign may be present and the defence reflex absent.

Mental Disorders Following Traumatism.

ALFRED GORDON (*New York Medical Journal*, September 20, 1922) writes that traumatism may be followed by mental disorders of a wide range. Extreme mental enfeeblement and neuroses, also considerable varieties of purely psychic disorders, have been observed. Among the latter confusion occupies a conspicuous place. Depression of all degrees, amnesia, slowness of psychic functions, simple confusion, delirium, epileptic phenomena and general paresis have all been observed between the two extremes of the pathological chain. A series of one hundred and twenty-six observations was grouped as follows: Twenty instances of a confusional state; twenty-five of amnesic phenomena; twenty-five of depression; seven of epilepsy; nine of general paresis; thirty of neuroses and seven of progressive mental enfeeblement. Considering these cases from the medico-legal aspect, it was shown that in eighteen out of the twenty patients suffering from a confusional state there was no fracture of the skull, but consciousness was lost in all. It was also shown that post-traumatic amnesia and depression may appear in all degrees; that in patients suffering from epilepsy inquiry should be made regarding syphilis or alcoholism, as well as a previous history of convulsive seizures; that trauma may precipitate general paresis; that *dementia præcox* and other progressive mental enfeeblement may also appear; and, lastly, that, not only must the relation between trauma and the various neuroses be kept in mind, but the so-called psychosis of vindication must be carefully sought.

Immobilization after Encephalitis.

KARL PETRÉN AND LEONARD BRAHME (*The Journal of Nervous and Mental Diseases*, February, 1923) observed an instance of *encephalitis lethargica* in which the patient suffered from almost complete immobilization of the body. Ocular, respiratory and swallowing movements alone were conserved. There was no true paralysis. It was in consequence of profound spasticity that neither voluntary nor passive movements could be performed. The limbs showed a patchy œdema. In another patient the immobility was unilateral and again due not to paralysis, but to hypertonia. In neither instance was the sign of Babinski present nor was there evidence of pyramidal tract involvement. In this second patient there was complete recovery of movement. In the first recovery of movement was only partial. It is assumed that the disability was produced by a lesion of the extrapyramidal motor system. In the first patient X-ray examination revealed changes suggestive of ossification in the soft tissues of both thighs and upper arms. These were apparently similar to those described by Madam Dejerine-Klumpke in patients with traumatic lesion of the spinal cord and it is believed that destruction of certain tracts of fibres was the cause.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne Hospital, on May 2, 1923, the President, DR. L. S. LATHAM, in the chair.

Leucocytes in Health and Disease.

DR. K. DOUGLAS FAIRLEY read a paper entitled "Leucocytes in Health and Disease" (see page 655).

DR. KONRAD HILLER, in opening the discussion, tendered his congratulations to Dr. Fairley on his extremely interesting paper. He had had the pleasure of reading the paper prior to the meeting and it was unfortunate that in the time allotted him Dr. Fairley was unable to present the whole of his work in detail. It was a good thing to take stock of knowledge from time to time and Dr. Fairley's review of present-day conceptions regarding hæmatogenesis, physiological and pathological conditions of the body, with special reference to the leucocytes, would well repay careful perusal.

Certain points emphasized by Dr. Fairley were new and would modify the interpretation hitherto placed on some of the findings in clinical hæmatology, as, for example, those of the differential leucocyte count. It had always been held that the normal polymorpho-nuclear lymphocyte ratio was approximately as seventy is to thirty, but they could not fail to accept Dr. Fairley's evidence that the more correct formula was 55: 45 and in view of this it was probable that the "relative lymphocytosis" to which so much importance was attached in various diseases, was of little value.

Dr. Fairley's presentation of the evolution of the white cells was simple and was therefore to be commended. He had given prominence to the work of Pappenheim and the new conception of hæmatogenesis which it involved, but at the same time the fundamental view of a common origin for the red and white cells and the recognition of three distinct types among the latter, granular, lymphocytic and endothelial, were not affected.

Dr. Fairley had discussed the fascinating subject of the theories regarding the mode of origin of leuchæmia and had adduced some evidence in support of the contention that the leuchæmic diseases were merely exaggerated responses on the part of the blood-forming tissues to some unknown toxic agents. He had also pointed out the difficulty attending the diagnosis of acute leuchæmia from acute infective lymphoblastosis and had stated that a low total leucocyte count was commonly observed in acute leuchæmia. The latter statement he (Dr. Hiller) could not support, as it was contrary to his experience. With Dr. Fairley he had occasionally been in difficulties in distinguishing acute infective lymphoblastosis from acute leuchæmia in an early stage, as two examples would illustrate.

In the first instance a young girl had become seriously ill, manifesting high fever, enlarged inguinal glands and by vaginal examination enlarged lymphatic glands in the pelvis. In a total leucocyte count of 30,000 cells per cubic millimetre the proportion of lymphocytes had been 85%. This patient had made a good recovery in the course of a few weeks.

The second example was furnished by man, aged thirty years, who had been very ill when first seen. Sloughing tonsillitis, enlarged lymphatic glands and splenomegaly had been obvious to clinical examination and the anterior border of the spleen had advanced to the umbilicus in the space of fourteen days. The total leucocyte count had been 12,000 cells per cubic millimetre and lymphocytes had been in great preponderance in the film. He had been deterred, however, from a diagnosis of leuchæmia by reason of the general appearance of the patient, who had not exhibited any appreciable degree of anæmia, and by the low leucocyte count. The patient had improved and subsequently got well under measures directed against the septic infection of the throat.

Dr. Hiller proceeded to remark that the infective theory of leuchæmia was very attractive and might ultimately prove correct, but for the present he found it difficult to understand how any specific infective agent could produce such varying tissue responses, lymphoblastic in one instance and myeloblastic in another.

The case record detailed by Dr. Fairley in which the total leucocyte count was 277,000 per cubic millimetre and comprised nearly 80% of neutrophile myelocytes just before death was very suggestive of infective leuchæmia.

In conclusion, Dr. Hiller recalled a paper read before the Branch a few months ago by Dr. E. A. Derrick, in which had been embodied admirable work on renal tumours carried out by Dr. Derrick during his tenure of the John Grice Cancer Research Scholarship. Under the facilities provided by the same scholarship Dr. Fairley had carried out another very valuable study. Both these papers had been most illuminating and had clarified the subjects with which they treated for all who had taken advantage of them. They served to show what excellent results were to be anticipated from the endowment of research, as had been realized by Sir John Grice.

DR. S. O. COWEN said that he wished to associate himself with Dr. Hiller's appreciation of Dr. Fairley's paper. Not only had Dr. Fairley given an exhaustive and authoritative survey of the recent literature of the subject, but those who had seen something of his work, realized the time and care he had lavished on the practical results embodied in the paper. His figures were impeccable and his statements as to the normal white counts were to be accepted without reserve.

His own figures for normal total and differential white counts were closely parallel to those of Dr. Fairley and he was quite in accord with his statement that a polymorpho-nuclear percentage of fifty and lymphocyte percentage of forty must be considered well within normal limits. The proportion of lymphocytes to polymorpho-nuclear cells might be 2: 1 in healthy children and in infants especially they should be very chary of drawing deductions from a supposed lymphocytosis.

Dr. Fairley had done well to lay stress on the close relationship between the infective hyper-leucocytoses and the leuchæmias.

He (Dr. Cowen) had seen several patients exhibiting this abnormal type of response to infection; in none of them, however, had the count of leucocytes been quite so striking as in the case detailed by Dr. Fairley. In the case of a child aged two and a half years in whom the principal clinical features had been very indefinite toxic mental symptoms, there had been found 43% of immature leucocytes, myelocytes and myeloblasts, in a total count of 12,600 per cubic millimetre. Nucleated red cells had also been numerous. There had been no clinical evidences of leuchæmia and the opinion had been offered that this was an instance of exaggerated response by the bone marrow to an infection. The only discoverable lesion found at autopsy had been an acute encephalitis, accompanied by evidence of toxic spoiling in other organs. It was worthy of note that these aberrant blood pictures in response to infection arose much more frequently in children than in adults.

Dr. Fairley had also very rightly emphasized the close relationship between the typical lymphatic leuchæmias and the local tumour-like growths of lymphoid tissue with or without leuchæmic blood. How close the relationship might be was illustrated by the case of a patient at present under observation.

Dr. Cowen displayed on the screen a graph illustrating the main features of this patient's blood count and from it was able to demonstrate the value of X-ray treatment in these conditions.

The man, aged sixty-five years, had come under Dr. Cowen's observation in March, 1919, suffering from digestive disturbances. No mention had been made in the notes of that date as to general or local glandular enlargement. Seven months later, however, the patient reappeared and there had been found a huge abdominal tumour stretching from the costal margin above to the pelvic brim below, filling the whole left side of the abdomen and extending below across the mid-line. The tumour had been distinct from the spleen and felt hard and nodular. The discovery of some hard, small glands in both axillæ had led Dr. Hiller to suspect the true state of affairs and a count showed 65,000 leucocytes per cubic millimetre, among which

there were 92% of lymphocytes. No glands had been palpable elsewhere and the local abdominal tumour had dominated the clinical picture. The case might quite reasonably have been regarded as one of leuchæmic lymphadenosis. (He thought, with Dr. Fairley, that this term of Webster was preferable to Longcope's lympho-cytoma.) The results of treatment were shown in the graph. Dr. Cowen attributed the improvement to the X-ray treatment rather than the benzol, which had been given in very small doses. The low figures reached at times emphasized the danger that a condition of leucocytic aplasia might occur with such treatment. It was remarkable that this enormous tumour disappeared within six months, even with the small doses of X-rays then being used. The main point of interest, however, was that after all the treatment the condition of the lymphatic glands had been typical of what was recognized as lymphatic leuchæmia rather than a tumour-like growth. In other words, there was general glandular enlargement affecting the axillary inguinal, cervical, mediastinal and possibly mesenteric glands, thus showing the very close relationship between the two conditions.

Dr. Cowen outlined an example of the so-called leucosarcoma of Sternberg which occurred in a boy of six years. A very large mediastinal tumour, apparently springing from the thymus and invading all the thoracic organs, had been associated with a white cell count of 250,000 per cubic millimetre, of which 98% had been lymphocytes. The liver, spleen and mesenteric glands had been somewhat increased in size, but there had been no general enlargement of the lymphatic glands.

Dr. Cowen said that such a case as the last mentioned made him wonder whether the relationship between the tumours and the leuchæmic group of diseases could be so easily dismissed as Dr. Fairley would have them believe. In both there was the same emancipation of one type of tissue from obedience to the laws which governed the growth of normal tissue, the same wild, unfederal overgrowth of embryonic cells. Dr. Fairley's chief objection to this point of view seemed to be in the multiple foci of growth in various organs and in the invasive rather than infiltrating character of these foci. Even if Pappenheim's theory were accepted as correct, that these local collections of lymphoid or myeloid cells were the product of local endothelial cells rather than true metastases, he could not see that either of these objections was valid. Further, to accept the view that there was much of the nature of tumour growth in the proliferation of lymphatic cells was not discordant with the evidence brought forward as to the close connexion with infective conditions. The process might well be started by an abnormal response to some metabolic or bacterial poison, but once under way the wild overgrowth of embryonic types of cell postulated a process entirely different from the response to any known intoxication.

Dr. Cowen concluded by saying that until further evidence could be adduced, he held that both elements, the neoplastic and the toxic, were to be borne in mind in a consideration of the ætiology of the lymph-adenoses.

DR. H. FLECKER said that he did not propose to discuss the issues raised by Dr. Fairley regarding the ætiology of leuchæmia, but wished to comment upon the therapeutic aspect of this disease in so far as it embraced irradiation.

As judged by the reports appearing from time to time in current medical literature, the effect of treatment of leuchæmia by X-rays was very much a matter of dosage. He recalled records published last year which showed that a patient affected with Hodgkin's disease who had been treated in 1915, was still alive and leading an active life. In another instance, a subject of leuchæmia treated in 1916 was still alive, but exhibited splenic enlargement. Another report related to the treatment of a lympho-sarcoma by radium; this had been carried out in 1913 and the patient was still alive. In each of these instances from one and a half to three grammes of radium had been employed, but such quantities were, of course, unobtainable in Australia.

Dr. Flecker referred to a patient in whom a tumour diagnosed histologically as a lymphoma had been removed surgically.

Within a short time the growth had recurred extensively and, being situated in the region of the pharynx, had interfered seriously with the patient's swallowing, respiration and hearing.

Under intensive X-ray treatment the tumour, although present for fourteen months, had disappeared in two weeks and eight months later there had been no recurrence.

Dr. Flecker suggested that light might be thrown on the problem of the infective or neoplastic nature of leuchæmia by breeding experiments on the lines by which Slye had succeeded in breeding strains of mice which could be relied upon to develope particular types of malignant disease.

DR. H. BOYD GRAHAM expressed his appreciation of Dr. Fairley's paper and said that in the course of his work at the Children's Hospital he had been able to follow many patients with acute leuchæmia through the whole course of the disease, from the early stages to autopsy. He had frequently observed a sub-leuchæmic phase and expressed surprise that such had not come within the experience of Dr. Hiller.

A remark of Dr. Hiller with reference to the association of anæmia with leuchæmia led him to the brief recital of the case record of a child formerly under the care of Dr. Forsyth at the Children's Hospital. The child had come under observation in April, 1922, when a severe anæmia and sub-leuchæmic state had been demonstrated. He had died of acute leuchæmia in August, 1922, but during the month preceding death the hæmoglobin percentage and red corpuscle counts had been high. This indicated that the anæmic and leuchæmic conditions had not progressed along parallel lines.

The occurrence of what appeared to be an aplastic state at varying stages in the development of a definite leuchæmia suggested to Dr. Graham that some examples of grave anæmia of the aplastic type without the features at present considered essential to the diagnosis of leuchæmia might in reality be examples of this disease. In a recent issue of THE MEDICAL JOURNAL OF AUSTRALIA Dr. Upjohn and he had reported a case history in which the aplastic condition had not proved fatal and the child later on had developed leuchæmia.

DR. A. J. TRINCA expressed his appreciation of Dr. Fairley's comprehensive paper and said that he had followed with interest the discussion of a possible infective agent or toxin as the underlying cause in lymphoblastosis and leuchæmia. As bearing on this question he outlined the case record of a patient in whom he had recovered a micro-organism from an excised gland. The patient, a rope worker, had been admitted to hospital by reason of a febrile illness in which the principal features had been troublesome cough and enlarged cervical glands which had been present for eighteen months. In the course of investigation a gland had been excised and he had subjected the tissue to culture in broth in which had appeared *Micrococcus catarrhalis* in pure culture.

Histological study of microscopical sections of the gland had disclosed a decided lymphoid hyperplasia as against reticulo-endothelial proliferation, which was considered as weighing against the provisional clinical diagnosis of Hodgkin's disease. In the routine blood examination secondary anæmia of moderate degree had been noted and it had been determined that 99% of the leucocytes present in the film were lymphocytes, chiefly of the small type. He had found one polymorpho-nuclear leucocyte only in a long search through two films.

Although there was a strong presumption in this instance that the lymphoblastosis was of infective origin, the ultimate proof of the infective theory of leuchæmia and the allied condition described by Dr. Fairley as acute infective lymphoblastosis was an extremely difficult problem.

DR. REGINALD WEBSTER said that in view of the turn taken by the discussion it might be of interest if he contributed some observations which at first seemed to have an important bearing on the infective nature of one of the diseases under discussion. He referred to Hodgkin's disease.

Some two years ago in the course of work at the Children's Hospital he had been afforded an opportunity of investigating an instance of this disease in a child in whom the clinical course had been unusually rapid; a space of four months had seen the beginning and the fatal termination. The diagnosis of Hodgkin's disease had been

established by repeated careful laboratory examinations of the blood and by the histological findings in the lymph glands before and after death.

Shortly after the child's admission he had carried out a blood culture and recovered a pure growth of a beaded, non-acid-fast diphtheroid bacillus which retained the stain in the Gram method of staining. In view of the great prominence that had been given to diphtheroid bacilli in association with Hodgkin's disease, the finding merited further investigation, especially as to the best of his knowledge the diphtheroid bacilli recorded as having been recovered in Hodgkin's disease had been isolated from the tissues and not as apparently in this case from the blood.

He therefore had attempted to communicate the disease to monkeys and had proceeded to inoculate two animals with the diphtheroid bacilli by every path of injection he could devise. These included the subcutaneous, intravenous, peri-glandular and intra-glandular routes. Results, however, had been obtained.

The scepticism with which he viewed the diphtheroid as a significant organism, was intensified by the recovery of a second diphtheroid bacillus staining by the Gram method from a mesenteric gland of the same patient *post mortem*. This organism, although it could rightly be described as a diphtheroid, exhibited distinct differences in morphology and sugar reactions from that which appeared in the blood culture.

Dr. Webster concluded by remarking that the activities and organisms of this nature were to be viewed with much reserve; diphtheroids were ubiquitous and were frequently encountered in skin lesions, in the male and female genitalia and in other situations. They had even been described by Ford Robertson as occurring in the cerebral tissues in general paralysis and the same writer had more recently connected aerobic and anaerobic diphtheroid bacilli with carcinomatous neoplasms.

DR. J. NEWMAN MORRIS said that he had found the subject of the evening, so admirably treated by Dr. Fairley, particularly interesting in view of the fact that two instances of acute lymphoblastosis had occurred in his practice a few months previously. Dr. Fairley had made reference to one of these and it would be of interest perhaps if he gave further details of the case.

A boy, aged nine years had become acutely ill with fever, sore throat and vomiting. Two days before he had been in such robust helath that he had run ninety times round a tennis court.

To clinical examination he had presented enlarged and tender cervical, axillary and inguinal glands and a distinctly enlarged spleen; the examination of the blood showed a total leucocyte count of 20,000 cells per cubic millimetre, 25% of which were polymorpho-nuclear cells and the remainder of lymphocytic, non-granular character. The boy's appearance was very suggestive of leuchæmia as the clinical diagnosis and this was supported by a pathologist's opinion on the blood film.

Two consultants had been of opinion that the boy was suffering from acute leuchæmia and that the prognosis was accordingly hopeless. The parents, in great distress, had cabled abstracts of the clinical facts to leading clinics on the other side of the world situated in London, New York, Berlin and Vienna. From the Mayo Clinic a report had been received to the effect that, although the disease would appear to be leuchæmia, there was a good probability that it was of the nature of an infective lymphoblastosis in which event recovery might be anticipated. When the help of Dr. S. W. Patterson had been sought, he had very kindly gone out to see the patient and with Dr. Fairley who had then been engaged on the work presented in his paper, had established the real nature of the disease.

Dr. Morris mentioned that within a week or two he was asked to see a second patient with infective lymphoblastosis and it was noteworthy from the point of view of the infective origin of this disorder that the two patients lived in neighbouring streets. This may have been no more than coincidence, but its possible significance had occasioned remark at the time. Both the patients got well and appeared likely to remain well. Practitioners were dependent on the clinical pathologist for the avoidance of stumbling blocks such as the two cases to which he had referred, and they should be very grateful to Dr. Fairley for a paper which would reconstruct their ideas and make them familiar with present day work and views on diseases of the blood.

DR. SYDNEY PERN said that the feature of Dr. Fairley's paper which interested him most, was the tendency it disclosed to regard the leuchæmias and allied conditions as of infective origin. Such a view fell into line with ideas he had for some time held on the subject, as after all, were any tissues immune from infection?

When bacteria gained access to a bodily tissue, if they did not produce hypofunction or actual destruction, their effect was to stimulate the component cells to hyperactivity and cell reproduction in such cells as were capable of reproduction as long as the irritant was present.

The relation between lymphoblastosis, leuchæmia, Hodgkin's disease and leuco-sarcoma would be seen in the response of the tissue cells in varying manner and degree to the action of some infecting agent.

For the purpose of presenting the conception it was not necessary to speculate on any specific infecting organism; there might well be a variety of bacteria capable of causing hypo- or hyper-function of the tissues invaded.

He wished to express his very great appreciation of Dr. Fairley's paper.

DR. A. GRAHAM BUTLER, D.S.O., drew attention to the fact that practically all the work undertaken in the past with the object of determining the origin and significance of the several types of leucocytes appearing in the blood under various conditions had been based upon the morphology and staining reactions of these cells.

He was not aware that investigations of normal and perverted functions of leucocytes had been carried out with anything like the minuteness which had been brought to bear upon their histology.

A great deal might be learned from a study of leucocytic functions; apart from the polymorpho-nuclear neutrophile cells very little was known of the actual causes of the large increase in the numbers of leucocytes which occurred under various circumstances.

Some years ago, in association with Dr. Froude Flashman, he had entered upon a study of the functions of leucocytes and in the preliminary stages they had directed their observations towards the property of phagocytosis as being well defined and easy to measure. They investigated the phagocytic powers of the polymorpho-nuclear cells, mononuclear cells, and of the very badly named "transitional" cells. (He had never been able to ascertain whether the cells bearing this name were transitional in respect of functions, structure, or staining reactions.) They had next proceeded to study the phagocytic qualities of the leucocytes present in three patients affected severally with acute "lymphatic," chronic lymphatic and splenomedullary leuchæmia.

Unfortunately, circumstances had intervened to prevent the work being carried to a stage at which conclusions might be drawn, but it had seemed to point to a profitable line of investigation.

Dr. Graham Butler made the suggestion that information as to the maturity or immaturity, pathological or physiological nature of leucocytes might be gained by investigation directed towards an estimate of their functions.

THE PRESIDENT congratulated Dr. Fairley and expressed his appreciation of the work involved in the preparation of such an exhaustive paper, the immediate result of which had been to evoke a very interesting discussion. To most of them it would bring a realization of the astonishing advances made in hæmatology since their student days and would stimulate their interest in the diverse and complex phenomena exhibited by the blood. It was apparent that the diseases of the blood and blood-forming organs could not now be fitted into the few compartments devised for them not many years ago.

With Dr. Hiller he had been impressed by the valuable results which had followed the endowment of research by Sir John Grice and it was to be hoped that more and more facilities for such work would be forthcoming in Melbourne.

In addition to the investigations which he had so patiently carried out, Dr. Fairley had attempted to unify prevailing conceptions regarding leuchæmia and related diseases and to bring these disorders into line by classi-

fying them as varying manifestations of the tissue response to infection, to the exclusion of the neoplastic element. The infective theory was fascinating and might ultimately be established, but on the other hand, Dr. Cowen had shown that there was a good deal to be said for the view which attributed certain of these diseases to the tumour process.

The Branch was to be congratulated on having been privileged to hear and discuss such an important contributon as that of Dr. Fairley.

DR. FAIRLEY, in reply, said that in the endeavour to accommodate his paper to the time at his disposal he had not amplified his statement that at the onset of acute leuchæmia the white cell count was practically always subleuchæmic, ranging from a few thousands to 30,000 per cubic millimetre, and that in a few instances it was aleuchæmic throughout the course of the disease.

Of the eleven patients with acute leuchæmia reviewed in the paper, four showed the total white count in the early stage to be under 30,000 per cubic millimetre, the lowest count recorded being 13,000 per cubic millimetre.

In an article on leuchæmia in the New Oxford Medicine, Ordway and Gorham, discussing the criteria for a diagnosis of acute leuchæmia, had laid great emphasis on the sub-leuchæmic phase of the disease in its early stages.

In conclusion, Dr. Fairley expressed his thanks to those who had contributed to the discussion.

NOMINATIONS AND ELECTIONS.

THE undermentioned has been nominated for election as a member of the New South Wales Branch of the British Medical Association:

TARLETON, ARTHUR, M.B., 1923 (Univ. Sydney), Baradine, New South Wales.

THE undermentioned has been elected a member of the South Australian Branch of the British Medical Association:

WEBB, ARTHUR LIDDON, M.B., B.S., 1922 (Univ. Adelaide), Adelaide Hospital.

THE undermentioned has been elected a member of the Queensland Branch of the British Medical Association:

FOOTE, LEONARD HARDWICK, M.B., Ch.M., 1922 (Univ. Sydney), Brisbane Hospital.

Correspondence.

OCCIPITO-POSTERIOR PRESENTATIONS.

SIR: In the case report by Dr. Donovan in THE MEDICAL JOURNAL OF AUSTRALIA, of June 2, 1923, there are a few points which need discussion; in fact, one feels that the statements were hardly meant.

The case in question was one of Cæsarean section on an elderly primipara on account of contracted pelvis and occipito-posterior presentation: the child weighed 2.5 kilograms, ". . . . disclosed a contraction in the middle of the pelvis and toward the outlet. The contraction was in the transverse diameter and was due to the fact that the ischia approached one another too closely." This description of a contracted pelvis which, in conjunction with an occipito-posterior presentation, necessitated Cæsarean section, is wanting in those important measurements and details by which one is able to judge the type and amount of contraction: without the four outlet measurements (antero-posterior, transverse, anterior and posterior sagittal) the diagonal conjugate and the amount of brim palpable, criticism of the conduct of the labour is rendered impossible.

Moreover, surely an error has been made when, in the discussion of this case, the statement occurs: "This type of contraction is unusual and would not be detected by ordinary antenatal examination and that external pelvimetry is useless in this type of deformity." For whatever type of bony contraction was present and Cæsarean section for a 2.5 kilogram child was indicated, then such contraction should be evident at an ordinary antenatal examination; for one of the chief functions of an antenatal examination is to exclude any contraction which would necessitate a Cæsarean section or to demonstrate the presence of a border-line pelvis: the situation of the contraction is immaterial.

Again, I do not agree to any internal interference of "occipito-posteriors" until the *os* is completely dilated: even in contracted pelves the majority deliver themselves if left alone.

In conclusion, may one suggest that the description of Munro Kerr's method of of judging the relative size of fœtal head and pelvis is not quite accurate.

Yours, etc.,

C. H. JAEDE.

Turramurra, New South Wales,
June 5, 1923.

THE MANUFACTURE OF GLANDULAR PRODUCTS.

IN the advertisement pages of this issue will be found some details of an undertaking of a well-known laboratory worker and bacteriologist, a member of the medical profession, who has rendered himself expert in the preparation of glandular products for therapeutic use. For some time a syndicate has been engaged under the title of Physiological Products Proprietary in manufacturing extracts of endocrine and other glands and in offering these products to the medical profession at reasonable prices. The extracts have been prepared with care under the direct supervision of the originator and each "line" has been accurately standardized as far as our knowledge at the present time admits of standardization. The syndicate, having passed successfully through the experimental stage, proposes to extend its sphere of operation and the extent of its usefulness. For this purpose a limited liability company is being formed. The medical profession is invited to make this a professional undertaking by acquiring the greater part of the property. The objects of the company are to provide the medical profession exclusively with delicate therapeutic agents and consequently it is to the advantage of the medical profession to have a controlling interest in the undertaking. The products are offered unconditionally to the profession. No patent rights are held and every medical practitioner can give his patients the benefit of treatment with these carefully prepared glandular extracts. While we cannot advise our readers as to the soundness from a financial point of view of this or any other investment, we commend the prospectus to the careful consideration of all.

Obituary.

HERBERT LETHINGTON MAITLAND.

OWING to the unusual length of Dr. Keith Fairley's important article in this issue, we have been compelled to delay the obituary notice of the late Herbert Lethington Maitland until next week.

Proceedings of the Australian Medical Boards.

TASMANIA.

The undermentioned have been registered, under the provisions of *The Medical Act*, 1918, as duly qualified medical practitioners:

GALBRAITH, JAMES BIGGAM DOUGLAS, M.B., Ch.B., 1917 (Glasgow), Campbell Town.

WALCH, JAMES HENRY BRETT, M.B., 1923 (Univ. Sydney), Hobart.

Books Received.

A MONOGRAPH ON GONORRHŒA, by A. Reith Fraser, M.D. (Aberd.); 1923. London: Henry Kimpton; Royal 8vo., pp. xvi. + 508, with 56 illustrations and 49 plates. Price 18s. net.

MEDICAL CLASSICS SERIES: TRANSLATION OF SELECTED PASSAGES FROM DE L'AUSCULATION MÉDIATE (FIRST EDITION), by R. Théophile H. Laennec, with a Biography by Sir William Hale-White, K.B.E., M.D.; 1923. London: John Bale, Sons and Danielsson, Limited; Crown 8vo., pp. ix. + 193, with ten illustrations. Price 12s. 6d. net.

Medical Appointments.

DR. D. T. R. SMITH (B.M.A.) has been appointed on probation Assistant Medical Officer at the Waterfall Sanatorium, New South Wales.

* * * *

DR. E. S. MORRIS (B.M.A.) has been appointed a member of the Returned Soldiers' Employment Board of Tasmania.

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DR. JOHN COFFEY (B.M.A.) has been appointed Deputy Commissioner of Public Health in Queensland during the absence of the Commissioner.

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The resignation of DR. J. J. D. HARRIS (B.M.A.) from the Directorship of the Laboratory of Micro-Biology and Pathology of the Department of Public Health of Queensland has been announced.

* * * *

THE undermentioned appointments have been made under the provisions of the *Lunacy Act*, 1915, of Victoria: DR. HENRY ROGERSON (B.M.A.), as Acting Superintendent of the Hospital for the Insane at Kew during the absence on leave of Dr. JOSEPH HOLLOW (B.M.A.); DR. ALBERT CURTIS (B.M.A.), as Superintendent of the Hospital for the Insane and of the Receiving House at Ballaarat during the absence on leave of DR. PATRICK SHAW (B.M.A.).

* * * *

DR. O. W. RAWSON (B.M.A.) has been appointed Public Vaccinator at Elmore, Victoria.

* * * *

DR. H. G. TYMMS (B.M.A.) has been appointed a Justice of the Peace for the State of Western Australia.

* * * *

DR. JOHN KENNY (B.M.A.) has been appointed District Medical Officer and Public Vaccinator at Roebourne, Western Australia.

* * * *

DR. A. J. MOLLISON (B.M.A.) and DR. E. W. B. WOODS (B.M.A.) have been appointed Government Medical Officers at Molong and Hay, respectively, in New South Wales.

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THE undermentioned appointments have been gazetted: DR. SINCLAIR GILLIES (B.M.A.) and DR. W. S. BROWN (B.M.A.), as Official Visitors to the Rydalmere Mental Hospital; SIR A. JARVIE HOOD (B.M.A.) and DR. ANDREW DAVIDSON (B.M.A.), as Official Visitors to the Licensed House for the Insane, Mount St. Margaret, Ryde, New South Wales.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xviii.

BROKEN HILL AND DISTRICT HOSPITAL: Senior Resident Medical Officer.

ROYAL AUSTRALIAN NAVY: Vacancies for Medical Officers.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429, Strand, London, W.C.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney	Australian Natives' Association Ashfield and District Friendly Societies' Dispensary Balmain United Friendly Societies' Dispensary Friendly Society Lodges at Casino Leichhardt and Petersham Dispensary Manchester Unity Oddfellows' Medical Institute, Elizabeth Street, Sydney Marrickville United Friendly Societies' Dispensary North Sydney United Friendly Societies People's Prudential Benefit Society Phœnix Mutual Provident Society
VICTORIA: Honorary Secretary, Medical Society Hall, East Melbourne	All Institutes or Medical Dispensaries Australian Prudential Association Proprietary, Limited Manchester Unity Independent Order of Oddfellows Mutual National Provident Club National Provident Association
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane	Brisbane United Friendly Society Institute Stannary Hills Hospital
SOUTH AUSTRALIA: Honorary Secretary, 12, North Terrace, Adelaide	Contract Practice Appointments at Renmark Contract Practice Appointments in South Australia
WESTERN AUSTRALIA: Honorary Secretary, Saint George's Terrace, Perth	All Contract Practice Appointments in Western Australia
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington	Friendly Society Lodges, Wellington, New Zealand

Diary for the Month.

JUNE 19.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JUNE 20.—Western Australian Branch, B.M.A.: Branch.
JUNE 20.—South Sydney Medical Association, New South Wales.
JUNE 21.—Brisbane Hospital for Sick Children: Clinical Meeting.
JUNE 22.—Queensland Branch, B.M.A.: Council.
JUNE 26.—New South Wales Branch, B.M.A.: Medical Politics Committee; Organization and Science Committee.
JUNE 27.—Victorian Branch, B.M.A.: Council.
JUNE 28.—South Australian Branch, B.M.A.: Branch.
JUNE 29.—New South Wales Branch, B.M.A.: Branch.
JULY 3.—New South Wales Branch, B.M.A.: Council (Quarterly).
JULY 4.—Victorian Branch, B.M.A.: Branch.
JULY 6.—Queensland Branch, B.M.A.: Branch.
JULY 10.—New South Wales Branch, B.M.A.: Ethics Committee.
JULY 11.—Western Australian Branch, B.M.A.: Council.
JULY 11.—Melbourne Pædiatric Society.
JULY 12.—Victorian Branch, B.M.A.: Council.
JULY 13.—New South Wales Branch, B.M.A.: Clinical Meeting.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, B.M.A. Building, 30-34, Elizabeth Street, Sydney. (Telephone: B. 4635.)

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